ACCESS DB # 182621

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PLEASE PRINT CLEARLY

Scientific and Technical Information Center

SEARCH REQUEST FORM

Requester's Full Name: MARCELA M CORDERO GARCIA Examiner #: 80381 Date: 3/20/06

Art Unit: 1654 Phone Number: 2-2939 Serial Number: 10/759,881

Location (Bldg/Room#): _____ (Mailbox #): _____ Results Format Preferred (circle): PAPER DISK

****

To ensure an efficient and quality search, please attach a copy of the cover sheet, claims, and abstract or fill out the following:

Title of Invention: METHOD FOR TREATING RHEUMATOID ARTHRITIS

Inventors (please provide full names): SEE ATTACHD BIB DS

Earliest Priority Date: 1/16/04

Search Topic:

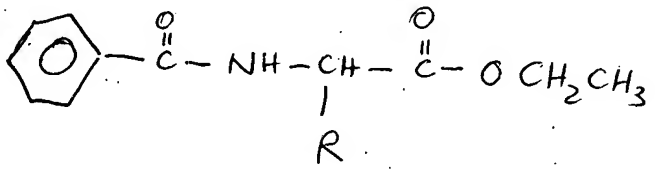
Please provide a detailed statement of the search topic, and describe as specifically as possible the subject matter to be searched. Include the elected species or structures, keywords, synonyms, acronyms, and registry numbers, and combine with the concept or utility of the invention. Define any terms that may have a special meaning. Give examples or relevant citations, authors, etc., if known.

For Sequence Searches Only *Please include all pertinent information (parent, child, divisional, or issued patent numbers) along with the appropriate serial number.*

C-Che
Rush

PLEASE SEARCH:

TREATING RHEUMATOID ARTHRITIS WITH



R=OPEN

OR WITH ANY COMPOUNDS CONTAINING A "BENZAMIDE" GROUP

IF NO OTHER WORK THAN APPLICANT'S,

PLEASE SEARCH BROADLY:

TREATING RHEUMATOID ARTHRITIS WITH A PAD (PEPTIDIL ARGININE DEIMINASE) INHIBITOR

****

STAFF USE ONLY

Searcher: Beverly C 25 28

Searcher Phone #: _____

Searcher Location: _____

Date Searcher Picked Up: _____

Date Completed: _____

Searcher Prep & Review Time: _____

Online Time: _____

Type of Search

_____ NA Sequence (#)

_____ AA Sequence (#)

_____ Structure (#)

_____ Bibliographic

_____ Litigation

_____ Fulltext

_____ Other

Vendors and cost where applicable

✓ STN _____ Dialog

_____ Questel/Orbit _____ Lexis/Nexis

_____ Westlaw _____ WWW/Internet

____ In-house sequence systems

___Commercial ___Oligomer ____Score/Length

___ Interference ___ SPDI ____ Encode/Transl

_____ Other (specify)

Cordero-Garcia
10/759881

FILE 'REGISTRY' ENTERED AT 10:26:29 ON 21 MAR 2006
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.

Property values tagged with IC are from the ZIC/VINITI data file provided by InfoChem.

STRUCTURE FILE UPDATES: 20 MAR 2006 HIGHEST RN 877371-73-8
DICTIONARY FILE UPDATES: 20 MAR 2006 HIGHEST RN 877371-73-8

New CAS Information Use Policies, enter HELP USAGETERMS for details.

TSCA INFORMATION NOW CURRENT THROUGH January 6, 2006

Please note that search-term pricing does apply when conducting SmartSELECT searches.

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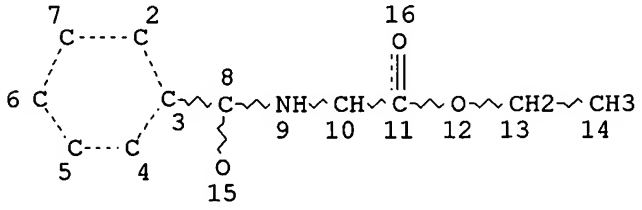
* *
* The CA roles and document type information have been removed from *
* the IDE default display format and the ED field has been added, *
* effective March 20, 2005. A new display format, IDERL, is now *
* available and contains the CA role and document type information. *
* *
****

Structure search iteration limits have been increased. See HELP SLIMITS for details.

REGISTRY includes numerically searchable data for experimental and predicted properties as well as tags indicating availability of experimental property data in the original document. For information on property searching in REGISTRY, refer to:

http://www.cas.org/ONLINE/UG/regprops.html

L1 STR



Str.

NODE ATTRIBUTES:
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 15

STEREO ATTRIBUTES: NONE
L2 3916 SEA FILE=REGISTRY SSS FUL L1

100.0% PROCESSED 69409 ITERATIONS 3916 ANSWERS

Searcher : Shears 571-272-2528

SEARCH TIME: 00.00.03

FILE 'CAPLUS' ENTERED AT 10:26:33 ON 21 MAR 2006
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
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FILE COVERS 1907 - 21 Mar 2006 VOL 144 ISS 13
FILE LAST UPDATED: 20 Mar 2006 (20060320/ED)

Effective October 17, 2005, revised CAS Information Use Policies apply.
They are available for your review at:

http://www.cas.org/infopolicy.html

L3 2708 SEA ABB=ON PLU=ON L2
L4 69 SEA ABB=ON PLU=ON L3 AND (RA(S)ARTHRITIS OR RHEUMATOID? OR ANTIARTHRIT? OR ANTIRHEUMAT?)
L5 53 SEA ABB=ON PLU=ON L4 AND (TREAT? OR THERAP? OR PREVENT?)

L6 19 SEA ABB=ON PLU=ON L5 NOT (PY=>2004 OR PD=>20040116) ← Restrict to only those items dated prior to 01-16-04

E1 THROUGH E72 ASSIGNED

L6 ANSWER 1 OF 19 CAPLUS COPYRIGHT 2006 ACS on STN
ED Entered STN: 11 Nov 2003
ACCESSION NUMBER: 2003:883028 CAPLUS
DOCUMENT NUMBER: 139:358808
TITLE: Pharmaceutical compositions for prophylactic and **therapeutic treatment** of diseases associated with α4 integrin-mediated cell adhesion
INVENTOR(S): Kawaguchi, Takayuki; Nomura, Sumihiro; Tsukumoto, Mikiko; Kume, Toshiyuki; Sircar, Ila
PATENT ASSIGNEE(S): Tanabe Seiyaku Co., Ltd., Japan
SOURCE: Jpn. Kokai Tokkyo Koho, 18 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
JP 2003321358	A2	20031111	JP 2003-51054		20030227
PRIORITY APPLN. INFO.:			JP 2002-51561	A	20020227

OTHER SOURCE(S): MARPAT 139:358808

Searcher : Shears 571-272-2528

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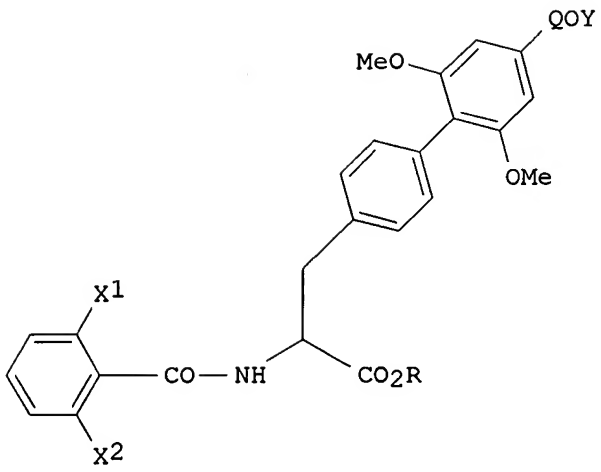

I

AB Title compns., useful for **treatment** of **rheumatoid** arthritis, asthma, allergy, inflammatory colon disease, multiple sclerosis, etc., contain phenylalanines I [X1, X2 = halo; Q = CH2, (CH2)2; Y = C1-6 alkyl; R = H, ester residue] or their pharmacol. acceptable salts as active ingredients. Thus, N-(2,6-dichlorobenzoyl)-4-(2,6-dimethoxy-4-n-propyloxymethylphenyl)-L-phenylalanine inhibited α4β7 integrin-mediated cell adhesion using RPMI8866 cell line with IC50 of 1.4 nM.

IT **402567-05-9P 402567-08-2P 402567-10-6P**
402567-12-8P 402567-14-0P 402567-17-3P
402567-19-5P 402567-20-8P 402567-23-1P
402567-26-4P 402567-28-6P 402567-29-7P
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(preparation of phenylalanines for **treatment** of diseases associated with α4 integrin-mediated cell adhesion)

IT **232276-71-0P 232276-72-1P 402567-40-2P**
402567-45-7P 402567-46-8P 402567-48-0P
402567-49-1P 402567-50-4P 402567-53-7P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of phenylalanines for **treatment** of diseases associated with α4 integrin-mediated cell adhesion)

L6 ANSWER 2 OF 19 CAPLUS COPYRIGHT 2006 ACS on STN
ED Entered STN: 02 Jan 2003
ACCESSION NUMBER: 2003:1275 CAPLUS
DOCUMENT NUMBER: 138:55866
TITLE: Preparation of indole derivatives as phospholipase enzyme inhibitors for **treatment** of inflammatory conditions
INVENTOR(S): Seehra, Jasbir S.; McKew, John C.; Lovering, Frank; Bemis, Jean E.; Xiang, Yibin; Chen, Lihren; Knopf, John L.

PATENT ASSIGNEE(S): Genetics Institute, LLC, USA
SOURCE: U.S., 57 pp., Cont.-in-part of U. S. Ser. No. 256,062, abandoned.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
US 6500853	B1	20021231	US 2000-686616		20001011
PRIORITY APPLN. INFO.:			US 1998-113674P	P	19980228
			US 1999-256062	B2	19990224

OTHER SOURCE(S): MARPAT 138:55866
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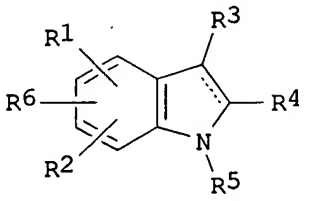

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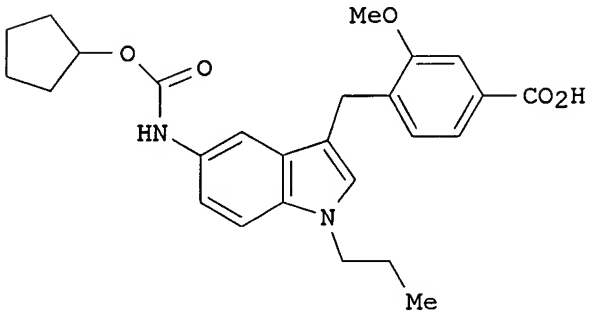


II

AB Title compds. I [wherein R1 and R6 = independently H, halo, CF3, alkyl, alkylthio, alkoxy, CN, NO2, NH2, Ph, OPh, SPh, CH2Ph, OCH2Ph, SCH2Ph, or (un)substituted amido, carbamido, sulfonyl, etc.; R2 = H, halo, CF3, OH, alkyl, alkoxy, CHO, CN, NO2, (un)substituted amino, or alkylsulfonyl; R3 = CO2H, OPO3H2, SO3H, etc.; R4 = H, CF3, alkyl, alkoxy, (alkyl)cycloalkyl, CHO, halo, etc.; R5 = alkyl, alkoxy, (alkyl)cycloalkyl, etc.; and pharmaceutically acceptable salts thereof] were prepared as phospholipase enzyme inhibitors. For example, 5-nitroindole was C3-alkylated (55%) with Me 4-(bromomethyl)-3-methoxybenzoate in dioxane, N-alkylated (57%) with 1-iodopropane in a solution of THF and NaH, and converted to the amine (80%) by hydrogenation using Pt/C. The amine was converted to the carbamate (39%) by addition of cyclopentyl chloroformate in CH2Cl2 and 4-methylmorpholine, and the resultant ester was hydrolyzed to yield II (71%). The latter inhibited cytosolic phospholipase A2 (cPLA2) by 50% at a concentration of 170 μM in a coumarin assay and reduced footpad volume by 16.61% at a dose of 5 mg/Kg IV in a carrageenan-induced footpad

edema test on rats. Thus, I are useful for **treatment** of inflammatory conditions, such as arthritis, inflammatory bowel disease, and asthma (no data).

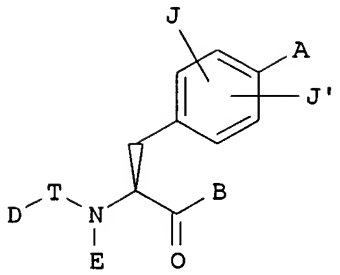
IT **241498-60-2**, Glycine, N-[4-[[6-chloro-1-(diphenylmethyl)-1H-indol-3-yl]methyl]-3-methoxybenzoyl]-, ethyl ester
RL: RCT (Reactant); RACT (Reactant or reagent).
(preparation of indole derivs. as phospholipase enzyme inhibitors for **treatment** of inflammatory conditions)

REFERENCE COUNT: 83 THERE ARE 83 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 3 OF 19 CAPLUS COPYRIGHT 2006 ACS on STN
ED Entered STN: 12 Apr 2002
ACCESSION NUMBER: 2002:275961 CAPLUS
DOCUMENT NUMBER: 136:310177
TITLE: Preparation of novel phenylalanine derivatives as inhibitors of integrin α4
INVENTOR(S): Suzuki, Nobuyasu; Yoshimura, Toshihiko; Izawa, Hiroyuki; Sagi, Kazuyuki; Makino, Shingo; Nakanishi, Eiji; Murata, Masahiro; Tsuji, Takashi
PATENT ASSIGNEE(S): Ajinomoto Co., Inc., Japan
SOURCE: PCT Int. Appl., 95 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
WO 2002028830	A1	20020411	WO 2001-JP8489		20010928
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM					
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG					
AU 2001090303	A5	20020415	AU 2001-90303		20010928
EP 1323711	A1	20030702	EP 2001-970268		20010928
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR					
US 2003220318	A1	20031127	US 2003-402006		20030331
PRIORITY APPLN. INFO.:			JP 2000-299490	A	20000929
			JP 2001-41885	A	20010219
			WO 2001-JP8489	W	20010928

OTHER SOURCE(S): MARPAT 136:310177
GI



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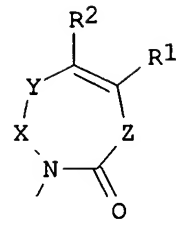
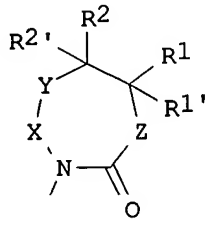
Q=



Q1=



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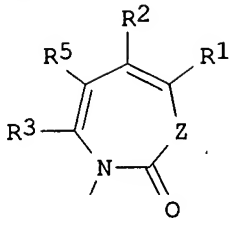

AB Specific phenylalanine derivs. (I) or pharmaceutically acceptable salts thereof [A = Q, Q1, Q2; X = CO, CR3R4; Y = bond, CR5R6, CR7:CR8, lower alkyl chain optionally containing 1 or 2 of O, S, or aromatic ring in the chain; Z = CR9R10, CR11R12CR13R14, lower alkyl or C2-3 alkylene chain optionally containing 1 or 2 of O, S, or aromatic ring in the chain;

R1

- R14, R1', R2' = H, lower alkyl, alkenyl, alkynyl, or cycloalkyl optionally containing a hetero atom in the ring, aryl, heteroaryl, cycloalkyl (optionally containing a hetero atom)-lower alkyl or -lower alkoxy, aryl-lower alkyl, heteroaryl-lower alkyl, lower alkoxy, lower alkoxycarbonyl, lower alkylcarbonyl, cyano,NO2, lower alkylsulfonyl, lower alkylsulfonylamino, etc.; B = HO, lower alkoxy, hydroxyamino; E = H, lower alkyl, alkenyl, or alkynyl, cycloalkyl (optionally containing a hetero atom in the ring)-lower alkyl, aryl-lower alkyl, heteroaryl-lower alkyl; D = lower alkyl, alkenyl, or alkynyl,lower alkoxy, hydroxyamino; E = H, lower alkyl, alkenyl, or alkynyl, cycloalkyl (optionally containing a hetero atom in the ring)-lower alkyl or -lower alkoxy, aryl-lower alkyl, heteroaryl-lower alkyl, lower alkoxy, aryl-lower alkoxy, heteroaryl-lower alkoxy, etc.; T = bond, COP, SO, SO2, NHCO, NHCS, CH2CO, CH:CHCO; J, J' = H, halo, lower alkyl, lower alkoxy, NO2] are prepared These compds. have an effect of inhibiting α4 integrin and, therefore, are useful as remedies or **preventives** for inflammatory diseases wherein the α4 integrin-dependent adhesion process participates in the pathol. conditions, for example, **rheumatoid** arthritis, inflammatory intestinal diseases, systemic lupus erythematosus, multiple sclerosis, Sjogren's disease, asthma, psoriasis, allergy, diabetes, cardiovascular diseases, arteriosclerosis, restenosis, tumor proliferation, tumor metastasis, and rejection in transplantation. Thus, a mixture of 2,6-dichloro-4-(5-tetrazolyl)benzoic acid 35, 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride 30, 1-hydroxybenzotriazole monohydrate 23, Et3N 15, and (2S)-2-amino-3-[4-(4-methyl-1,3-dioxo-1,3-dihydroisoindol-2-yl)phenyl]propionic acid Et ester hydrochloride 35 mg in 5 mL CH2Cl2 was stirred at room temperature for 3 days, followed by **treatment**

with a mixture of 4 N HCl/dioxane and H2O to (2S)-2-((2,6-dichloro-4-(5-tetrazolyl)benzoyl)amino)-3-[4-(4-methyl-1,3-dioxo-1,3-dihydroisoindol-2-yl)phenyl]propionic acid (II). II in vitro inhibited the binding of VCAM-1 to human T-cell Jurkat expressing integrin α4β1 and that of VCAM-1 to human lymphoma B cell expressing integrin α4β7 with IC50 of 0.0059 and 0.00055 μM, resp.

IT **409127-28-2P 409127-29-3P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of phenylalanine derivs. as inhibitors of integrin α4 and remedies or **preventives** for inflammatory diseases)

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 4 OF 19 CAPLUS COPYRIGHT 2006 ACS on STN
ED Entered STN: 03 Apr 2001
ACCESSION NUMBER: 2001:232516 CAPLUS
DOCUMENT NUMBER: 134:275760
TITLE: Medicine compositions for **treatment** of integrin α4-mediated cell adhesion-associated diseases
INVENTOR(S): Sircar, Ila; Gudmundsson, Kristjan S.; Martin, Richard
PATENT ASSIGNEE(S): Tanabe Seiyaku Co., Ltd., Japan
SOURCE: Jpn. Kokai Tokkyo Koho, 88 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 2001089368	A2	20010403	JP 2000-216898	20000718
PRIORITY APPLN. INFO.:			JP 1999-204581 A	19990719

OTHER SOURCE(S): MARPAT 134:275760
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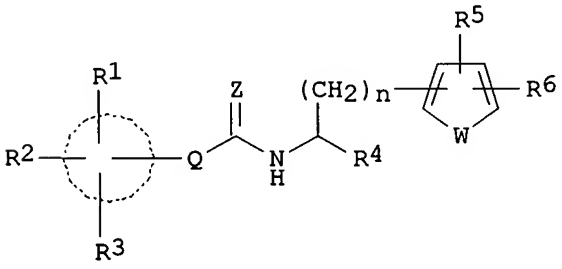

I

AB The medicine compns. (I; A = aromatic hydrocarbon ring; Q = binding linkage; N = 0, 1, 2; W = O, S, -CH=CH-, -N=CH-; Z = O, S; R1, R2, R3 = H, halogen, (substituted)low alkyl; R4 = tetrazolyl, carboxyl, etc.; R5 = H, nitro, (substituted)amino, OH low alkanoyl, etc.; R6 = (substituted)phenyl, etc.) and their pharmacol: acceptable salts are claimed for **treatment** of integrin 4-mediated cell

adhesion-associated diseases, including asthma, diabetes, **rheumatoid** arthritis, inflammatory bowel disease, and digestive tract and other diseases associated with leukocyte infiltration in the epithelium (e.g. skin, urethra, bronchiole, synovial membrane and transplanted kidney, liver, heart, blood vessel, and nerve tissues, and pancreas and other diseases including psoriasis, atopic dermatitis, contact dermatitis, systemic lupus erythematosus, etc.). I were prepared, and their inhibitory effects on cell adhesion were tested in vitro.

IT **232274-09-8P 232274-27-0P 232274-28-1P**
232274-31-6P 232275-24-0P 232275-26-2P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(phenylalanine analogs as medicine compns. for **treatment** of integrin α4-mediated cell adhesion-associated diseases)

L6 ANSWER 5 OF 19 CAPLUS COPYRIGHT 2006 ACS on STN
ED Entered STN: 13 Nov 1998
ACCESSION NUMBER: 1998:721702 CAPLUS
DOCUMENT NUMBER: 129:330743
TITLE: Preparation of phosphodiesterase 4-inhibiting [1,4]diazepino[6,7,1-hi]indol-4-ones
INVENTOR(S): Pascal, Yves; Burnouf, Catherine; Gaudilliere, Bernard; Jacobelli, Henry; Calvet, Alain; Payne, Adrian; Dahl, Svein Gunwald
PATENT ASSIGNEE(S): Jouveinal, Fr.
SOURCE: PCT Int. Appl., 79 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9849169	A1	19981105	WO 1998-EP2827	19980430
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, GW, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
FR 2762841	A1	19981106	FR 1997-5422	19970430
FR 2762841	B1	19990702		
HR 980231	B1	20020630	HR 1998-980231	19980429
CA 2278217	AA	19981105	CA 1998-2278217	19980430
AU 9877652	A1	19981124	AU 1998-77652	19980430
ZA 9803704	A	19991025	ZA 1998-3704	19980430
EP 980374	A1	20000223	EP 1998-925598	19980430
EP 980374	B1	20030212		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
BR 9809429	A	20000613	BR 1998-9429	19980430
NZ 337589	A	20001027	NZ 1998-337589	19980430

JP 2001522367	T2	20011113	JP 1998-546624		19980430
AT 232534	E	20030215	AT 1998-925598		19980430
ES 2190083	T3	20030716	ES 1998-925598		19980430
US 6239130	B1	20010529	US 1999-380883		19991110
PRIORITY APPLN. INFO.:			FR 1997-5422	A	19970430
			WO 1998-EP2827	W	19980430

OTHER SOURCE(S): MARPAT 129:330743

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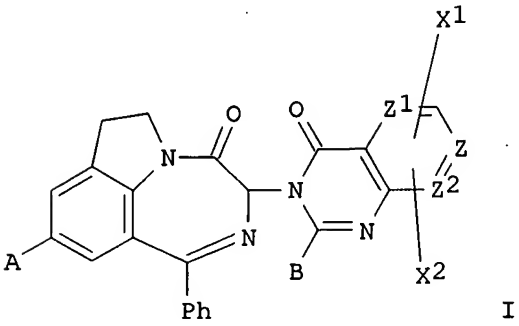


I

AB The title compds. [I; A = H, C1-4 alkyl, alkoxy, OH, NO2, (un)substituted NH2, etc.; B = alkyl, CH2OM, CH2O2C(CH2)a(CO)bY1Y2, (CH2)cCO2M; Y1 = (VCH2CH2)c, NHCHR(CO); M = alkyl, H; V = NH, O; R = residue of a natural α-amino acid with the C atom to which it is linked having a (R) or (S) configuration; Y2 = H, OH, OMe, 4-morpholinyl; a = 1, 2; b = 0, 1; c = 0-2; X1, X2 = H, alkyl, halogen, CN, (un)substituted 5-tetrazolyl, etc.; Z = CH when Z1 and Z2 are CH or N, Z = N when Z1 and Z2 are CH], useful in the **treatment** of phosphodiesterase 4-mediated diseases [e.g., asthma, atopic dermatitis, **rheumatoid** arthritis, inflammatory bowel disorders, pulmonary hypertension, liver injury, bone loss, etc. (all no data)], are prepared and I-containing formulations presented. Thus, (3R)-3-amino-1-phenyl-6,7-dihydro-3H-[1,4]diazepino[6,7,1-hi]indol-4-one was reacted with 2-acetamidobenzoic acid in the presence of O-[(ethoxycarbonyl)cyanomethylamino]-N,N,N',N'-tetramethyluronium tetrafluoroborate, and the intermediate reacted with 1,1,1-trimethoxyethane and cyclized, producing (3S)-3-(2-methyl-4-oxo-4H-quinazolin-3-yl)-1-phenyl-6,7-dihydro-3H-[1,4]diazepino[6,7,1-hi]indol-4-one which demonstrated a phosphodiesterase 4-inhibiting activity of 0.448 (using an enzyme preparation from the U937 cell line), vs. 0.792 for rolipram.

IT **215105-57-0P**

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of phosphodiesterase 4-inhibiting [1,4]diazepino[6,7,1-hi]indol-4-ones)

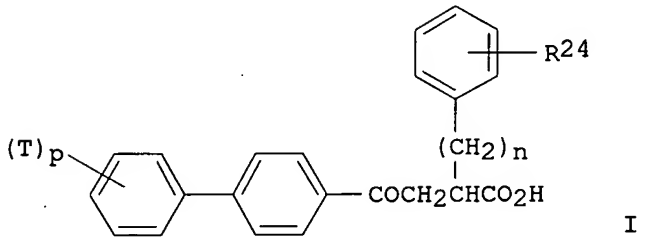
REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 6 OF 19 CAPLUS COPYRIGHT 2006 ACS on STN

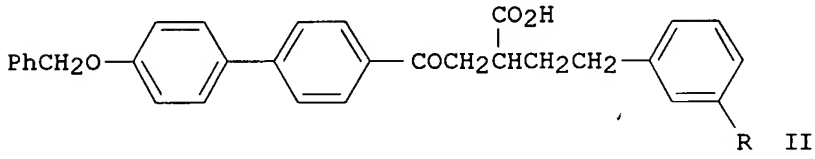
ED Entered STN: 17 Sep 1998
ACCESSION NUMBER: 1998:590737 CAPLUS
DOCUMENT NUMBER: 129:230536
TITLE: Inhibition of matrix metalloproteases by substituted phenalkyl compounds
INVENTOR(S): Wolanin, Donald J.
PATENT ASSIGNEE(S): Bayer Corp., USA
SOURCE: U.S., 22 pp.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5804581	A	19980908	US 1997-856696	19970515
PRIORITY APPLN. INFO.:			US 1997-856696	19970515

OTHER SOURCE(S): MARPAT 129:230536
GI



I



II

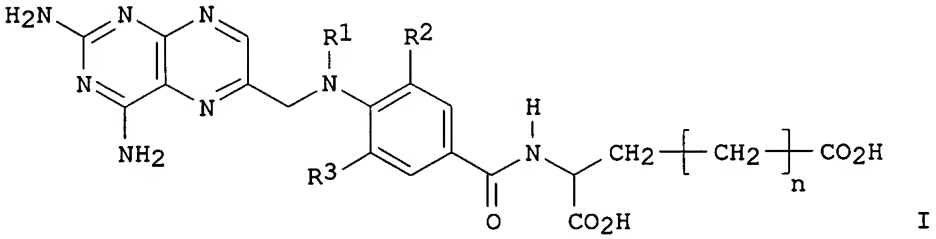
AB Matrix metalloprotease inhibiting compds., pharmaceutical compns. thereof and a method of disease **treatment** using such compds. are presented. The compds., i.e. 2-phenylalkyl-4-(1,1'-biphenyl-4-yl)-3-oxobutyric acid, of the invention have the generalized formula [I; T = halo, benzyloxy, C1-5 alkoxy; p = 1,2; n = an integer of 1-5; R24 = morpholinocarbonyl, N-(2-morpholinoethyl)carbamoyl, N-(3-phenylpropyl)carbamoyl, N-(2-phenylethyl)carbamoyl, N-(2-ethoxycarbonylethyl)carbamoyl, N-(ethoxycarbonylmethyl)carbamoyl, N-(2-carboxyethyl)carbamoyl, etc.]. These compds. are useful for inhibiting matrix metalloproteases and, therefore, combating conditions to which MMP's contribute, such as osteoarthritis, **rheumatoid** arthritis, septic arthritis, periodontal disease, corneal ulceration, proteinuria, aneurysmal aortic disease, dystrophobic epidermolysis, bullosa, conditions leading to inflammatory responses, osteopenias mediated by MMP activity, tempera mandibular joint disease, demyelating diseases of the nervous system, tumor metastasis or degenerative cartilage loss following traumatic

joint injury, and coronary thrombosis from atherosclerotic plaque rupture. The present invention also provides pharmaceutical compns. and methods for **treating** such conditions.
Palladium-mediated carbonylation of 4-(3-iodophenyl)butyric acid derivative (II; R = iodo) by carbon monoxide and piperidine as the nucleophile in the presence of Pd(OAc)2 and 1,3-bis(diphenylphosphino)propane in DMSO gave the title compound II (piperidine-1-carbonyl), which inhibited MMP-3, MMP-9, and MMP-2 with Ki of 12.5, 102, and 4.44 nM, resp.

IT **199674-64-1P 199674-74-3P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of phenylalkyl(biphenylyl)oxobutyric acid derivs. as inhibitors of matrix metalloproteases for **treating** matrix metalloproteases-associated diseases)

REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 7 OF 19 CAPLUS COPYRIGHT 2006 ACS on STN
ED Entered STN: 15 Jan 1997
ACCESSION NUMBER: 1997:22487 CAPLUS
DOCUMENT NUMBER: 126:157483
TITLE: **Antirheumatic** agents. II. Novel methotrexate derivatives bearing in alkyl-substituted benzene ring
AUTHOR(S): Matsuoka, Hiroharu; Maruyama, Noriaki; Suzuki, Hiroshi; Kuroki, Toshio; Tsuji, Keiichiro; Kato, Nobuaki; Ohi, Nobuhiro; Mihara, Masahiko; Takeda, Yasuhisa; Yano, Keiichi
CORPORATE SOURCE: Fuji-Gotemba Lab., Chugai Pharm. Co. Ltd., Shizuoka, 412, Japan
SOURCE: Chemical & Pharmaceutical Bulletin (1996), 44(12), 2287-2293
CODEN: CPBTAL; ISSN: 0009-2363
PUBLISHER: Pharmaceutical Society of Japan
DOCUMENT TYPE: Journal
LANGUAGE: English
GI



I

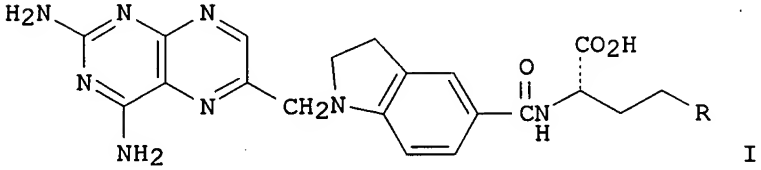
AB Novel methotrexate (MTX) derivs. I (R1-R3 = H, Me, etc.; n = 1-2) with either a mono- or dialkyl-substituted benzene rings were synthesized and initially tested for in vitro anti-proliferative activities using human peripheral blood mononuclear cells (hPBMC) derived from healthy

volunteers and synovial cells (hSC) derived from patients with **rheumatoid arthritis** (**RA**). Compds. with potent activities were further evaluated in an in vivo adjuvant arthritis model. In comparison with MTX, a glutamate derivative I (R1 = Me, R2 = Me, R3 = H, n = 1) was more potent as a suppressor of the in vitro cell proliferation and in vivo exptl. arthritis. Homoglutamate derivative, I (R1 = Me, R2 = Me, R3 = H, n = 2), exhibited fairly good activities in vitro and considerable activity in vivo in a dose-dependent manner. As expected, I (R1 = Me, R2 = Me, R3 = H, n = 2) did not act as a substrate for folylpolyglutamate synthetase (FPGS), and thus did not undergo polyglutamation, which is thought to be responsible for side-effects that occur during MTX **therapy**
.

IT **126632-37-9P 126632-47-1P 153304-23-5P**
153304-25-7P 153304-32-6P 153304-41-7P
153304-47-3P 153304-48-4P 153304-51-9P
153304-62-2P 153304-63-3P 186810-07-1P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of methotrexate derivs. as **antirheumatic** drugs)

REFERENCE COUNT: 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 8 OF 19 CAPLUS COPYRIGHT 2006 ACS on STN
ED Entered STN: 30 Jul 1996
ACCESSION NUMBER: 1996:448002 CAPLUS
DOCUMENT NUMBER: 125:222372
TITLE: **Antirheumatic** agents. I. Novel methotrexate derivatives bearing an indoline moiety
AUTHOR(S): Matsuoka, Hiroharu; Kato, Nobuaki; Tsuji, Keiichiro; Maruyama, Noriaki; Suzuki, Hiroshi; Mihara, Masahiko; Takeda, Yasuhisa; Yano, Keiichi
CORPORATE SOURCE: Fuji-Gotemba Lab., Chugai Pharmaceutical, Co., Ltd., Shizuoka, 412, Japan
SOURCE: Chemical & Pharmaceutical Bulletin (1996), 44(7), 1332-1337
CODEN: CPBTAL; ISSN: 0009-2363
PUBLISHER: Pharmaceutical Society of Japan
DOCUMENT TYPE: Journal
LANGUAGE: English
GI



I

AB Various novel methotrexate (MTX) derivs. I (R = CH2NHCOC6H4R1, CH2CO2H, SO3H, CO2H; R1 = 2-, 3-, or 4-CO2H) bearing an indoline moiety were synthesized and tested for biol. activities using human

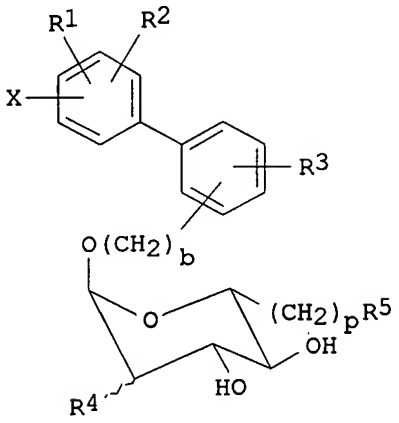
peripheral blood mononuclear cell and human synovial cells derived from patients with **rheumatoid** arthritis. Compds. having potent activity in vitro were further evaluated using an adjuvant arthritis model in vivo. I (R = CO2H) showed more potent activities than MTX in vitro and in vivo, and I (R = CH2CO2H) exhibited fairly good activities in vitro and considerable activity in vivo. I (R= CH2CO2H) was, as expected, not sensitive to folyl-polyglutamate synthetase and did not undergo polyglutamation, a process which may be responsible for a side-effect during MTX **therapy**.

IT **142165-64-8P 142165-65-9P 142166-12-9P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of **antirheumatic** methotrexate derivs. bearing an indoline moiety)

L6 ANSWER 9 OF 19 CAPLUS COPYRIGHT 2006 ACS on STN
ED Entered STN: 26 Sep 1995
ACCESSION NUMBER: 1995:810934 CAPLUS
DOCUMENT NUMBER: 124:56563
TITLE: Preparation of biphenylyl monosaccharide glycosides as inhibitor of binding of E-selectin or P-selectin to sialyl Lewisx or sialyl-Lewisa
INVENTOR(S): Kogan, Timothy P.; Dupre, Brian; Scott, Ian L.; Keller, Karin; Dao, Huong; Beck, Pamela J.
PATENT ASSIGNEE(S): Texas Biotechnology Corporation, USA
SOURCE: U.S., 23 pp.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5444050	A	19950822	US 1994-235293	19940429
CA 2189013	AA	19951109	CA 1995-2189013	19950428
WO 9529682	A1	19951109	WO 1995-US5463	19950428
W: AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LT, LU, LV, MD, MG, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TT				
RW: KE, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9524329	A1	19951129	AU 1995-24329	19950428
AU 691920	B2	19980528		
EP 758243	A1	19970219	EP 1995-918365	19950428
EP 758243	B1	20030312		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
CN 1151117	A	19970604	CN 1995-193539	19950428
BR 9507561	A	19970805	BR 1995-7561	19950428
JP 09512560	T2	19971216	JP 1995-528493	19950428
AT 234102	E	20030315	AT 1995-918365	19950428
NO 9604566	A	19961230	NO 1996-4566	19961028
TW 457246	B	20011001	TW 1996-85115658	19961219
PRIORITY APPLN. INFO.:			US 1994-235293 A	19940429
			WO 1995-US5463 W	19950428

OTHER SOURCE(S): MARPAT 124:56563
GI



I

AB The title compds. [I; X = (CH2)nCO2H, O(CH2)mCO2H, (CH2)nO(CH2)mCO2H, CONH(CH2)mCO2H, CH(OZ)CO2H, CH(Z)CO2H, (CH2)nSO3H, (CH2)nPO3D1D2, NH(CH2)mCO2H, CONH(CHR6)CO2H, 1-H-tetrazolyl-5-alkyl, OH; R1, R2 = H, alkyl, halo, OZ, NO2, NH2, NHZ; R3 = H, halo, alkyl, OZ, NHZ; R4 = H, halo, alkyl, OH, hydroxyl-O-sulfate, OZ; R5 = HO, cyano, N3, NH2, NHNH2, NE1E2, NHE1, NHCO(CH2)nCO2H, S(CH2)mCO2H, NHCHNHNH2; R6 = H, alkyl, aralkyl, hydroxyalkyl, aminoalkyl, alkyl, carboxylic acid, alkyl carboxamide; wherein n = 0-6; m = 1-6; p = 0-6; b = 0-2; Z = alkyl, aryl or aralkyl; D1, D2 = H, alkyl; E1 = alkyl, (CH2)8CO2H; E2 = alkyl] and the pharmaceutically acceptable salts, esters, amides, and prodrugs thereof are prepared This invention also relates to methods of inhibiting the binding of E-selectin and/or P-selectin to sialyl-Lewisx or sialyl-Lewisa presented on a cell surface using said compds. and to pharmaceutically active compns. comprising compds. that inhibit the binding of E-selectin to sialyl-Lewisx and to methods of **treatment** of septic shock, adult respiratory distress syndrome (ARDS), Crohn's disease, chronic inflammatory diseases, such as psoriasis and **rheumatoid** arthritis, and reperfusion injuries that occur following heart attacks, strokes and organ transplants (no data). Thus,.

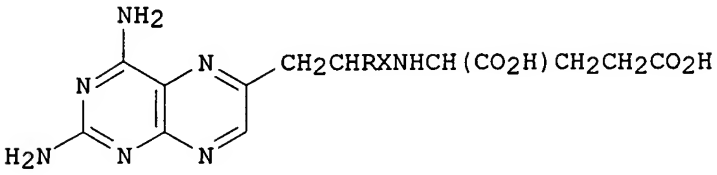
IT **171905-67-2P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of biphenylyl monosaccharide glycosides as inhibitors of binding of E-selectin or P-selectin to sialyl Lewisx or sialyl-Lewisa)

L6 ANSWER 10 OF 19 CAPLUS COPYRIGHT 2006 ACS on STN
ED Entered STN: 23 Nov 1994
ACCESSION NUMBER: 1995:205964 CAPLUS
DOCUMENT NUMBER: 122:240437
TITLE: Heteroaroyl 10-deazaamino-pterine compounds and use for **rheumatoid** arthritis and other proliferative diseases
INVENTOR(S): Degraw, Joseph I.; Colwell, William T.; Sirotnak, Francis M.; Smith, R. Lane; Piper, James R.

PATENT ASSIGNEE(S): SRI International, USA
SOURCE: U.S., 24 pp. Cont.-in-part of U.S. Ser. No. 28,431.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 6
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5354751	A	19941011	US 1993-90750	19930712
US 5374726	A	19941220	US 1993-28431	19930309
US 5536724	A	19960716	US 1993-140793	19931021
PRIORITY APPLN. INFO.:			US 1992-845407 B2	19920303
			US 1992-875779 B2	19920429
			US 1992-938105 B2	19920831
			US 1993-8919 A2	19930126
			US 1993-28431 A2	19930309
			US 1993-90750 A2	19930712

OTHER SOURCE(S): MARPAT 122:240437
GI



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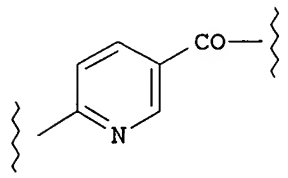
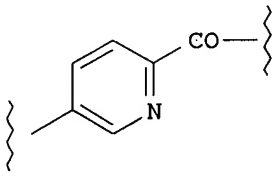


II



III

AB There is disclosed certain heteroaroyl 10-deazaaminopterin (I; X = one of II or III; R = H or alkyl, alkenyl, or alkynyl have from 1 to 8 C atoms) and 5,10- and 8,10-dideazaminopterin compds. and their use for **treatment** of **rheumatoid** arthritis and related diseases and preparative process. Also disclosed are 10-alkenyl(and alkynyl)-10-deazaminopterins for **treatment** of **rheumatoid** arthritis and for leukemia and ascites tumors and preparative process. **Antiarthritic** activity in mice was assessed by visually observed presence of inflammation and caliper-measured degree of paw swelling: the number of mice affected by disease was considerably decreased by administration of I (e.g., 4/8 affected, 2.19-2.35 paw thickness vs. 41/43 affected, 2.29-2.73 paw

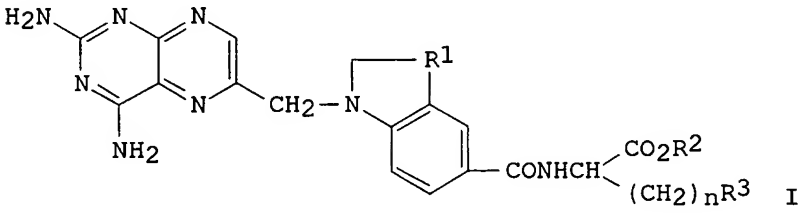
thickness for 10-allyl-10-deazaaminopterin at 12 mg/kg dose). Growth inhibition of leukemia cells (IC50 nM): 10-allyl-10-deazaaminopterin (4.30), 10-propargyl-10-deazaaminopterin (2.0). Antitumorigenic affect of 10-propargyl-10-deazaaminopterin: at 36 mg/kg, total suppression of growth of tumor at 14 and 21 day post-**treatment** points. Pharmaceutical formulations are given.

IT **146464-94-0P 162368-25-4P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(heteroaroyl 10-deazaaminopterin compds. and use for **rheumatoid** arthritis and other proliferative diseases)

L6 ANSWER 11 OF 19 CAPLUS COPYRIGHT 2006 ACS on STN
ED Entered STN: 03 Sep 1994
ACCESSION NUMBER: 1994:499796 CAPLUS
DOCUMENT NUMBER: 121:99796
TITLE: Preparation of pteridinylindolines for **treatment** of rheumatism
INVENTOR(S): Matsuoka, Koji; Kato, Nobuaki; Myamoto, Katsuhito; Ooi, Nobuhiro; Tsuji, Keiichiro; Suzuki, Yasushi; Takeda, Yasuhisa; Mihara, Masahiko
PATENT ASSIGNEE(S): Chugai Pharmaceutical Co Ltd, Japan
SOURCE: Jpn. Kokai Tokkyo Koho, 38 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 06016558	A2	19940125	JP 1993-64582	19930212
JP 3281099	B2	20020513		
PRIORITY APPLN. INFO.:			JP 1992-75107 A1	19920213

OTHER SOURCE(S): MARPAT 121:99796
GI



AB Pteridine derivs. [I; R1 = CH2, CH2CH2, CH2O, CH2S, CH2SO; R2 = H, C1-4 alkyl, benzyl; n = 1-4, R3 = COOR4, NHCOR5, CONR6N7, PO3H2, SO3H; R4 = H, C1-4 alkyl; R5 = (un)substituted Ph; R6 = H, C1-4 alkyl; R7 = H, C1-4 alkyl, Ph, etc] are prepared for **treatment** of rheumatism. For example, I (R1 = CH2, R2 = H, n = 2, R3 = COOH) was prepared and tested for its **antirheumatism** activity by determining the inhibitory activity against lymph proliferation in vitro.

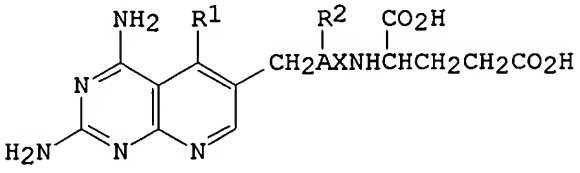
IT **142165-64-8P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation and decarbobenzoxylation of)

IT **142165-65-9P 142166-10-7P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and reaction of, with (bromomethyl)diaminopteridine)
IT **142166-12-9P 142166-32-3P 142166-34-5P 156578-93-7P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of, for **treatment** of rheumatism)

L6 ANSWER 12 OF 19 CAPLUS COPYRIGHT 2006 ACS on STN
ED Entered STN: 28 May 1994
ACCESSION NUMBER: 1994:270438 CAPLUS
DOCUMENT NUMBER: 120:270438
TITLE: Deazaaminopterins for **treatment** of inflammatory diseases
INVENTOR(S): Piper, James R.; Degraw, Joseph I.; Colwell, William T.; Sirotnak, Francis M.; Smith, R. Lane
PATENT ASSIGNEE(S): SRI International, USA
SOURCE: PCT Int. Appl., 67 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 6
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
WO 9322312	A1	19931111	WO 1993-US3965		19930428
W: AU, CA, JP, KR					
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE					
AU 9342201	A1	19931129	AU 1993-42201		19930428
EP 638079	A1	19950215	EP 1993-910852		19930428
EP 638079	B1	19991215			
R: DE, FR, GB, IT, NL					
JP 07506369	T2	19950713	JP 1993-519472		19930428
PRIORITY APPLN. INFO.:			US 1992-875779	A	19920429
			US 1993-8919	A	19930126
			WO 1993-US3965	A	19930428

OTHER SOURCE(S): MARPAT 120:270438
GI



I

AB The title compds. I (A = CH, N; R1, R2 = H, alkyl, alkenyl, alkynyl; X = 1,4-C6H4CO, heterocyclylcarbonyl), useful in the **treatment** of inflammatory diseases such as **rheumatoid** arthritis, are prepared and I-containing formulations presented. Thus, N-[5-[[(2,4-diaminopyrido[2,3-d]pyridin-6-yl)methyl]amino]thiophene-2-

carbonyl]-L-glutamic acid was prepared from 6-(bromomethyl)-2,4-diaminopyrido[2,3-d]pyrimidine.

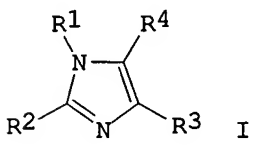
IT **153802-63-2 153802-68-7**
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation as intermediate in preparation of deazaaminopterine antiinflammatory agents)

IT **13726-52-8**
RL: RCT (Reactant); RACT (Reactant or reagent)
(reactant, in preparation of deazaaminopterins antiinflammatory agents)

L6 ANSWER 13 OF 19 CAPLUS COPYRIGHT 2006 ACS on STN
ED Entered STN: 08 Jan 1994
ACCESSION NUMBER: 1994:8592 CAPLUS
DOCUMENT NUMBER: 120:8592
TITLE: Pyridyl-substituted imidazoles with cytokine-suppressive properties
INVENTOR(S): Adams, Jerry Leroy; Gallagher, Timothy Francis; Garigipati, Ravi Shanker
PATENT ASSIGNEE(S): SmithKline Beckman Corp., USA
SOURCE: PCT Int. Appl., 38 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9314082	A1	19930722	WO 1993-US675	19930113
W: AU, CA, JP, KR, US				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
AU 9335924	A1	19930803	AU 1993-35924	19930113
EP 624159	A1	19941117	EP 1993-904625	19930113
EP 624159	B1	19981125		
R: BE, CH, DE, FR, GB, IT, LI, NL				
JP 07503018	T2	19950330	JP 1993-512742	19930113
JP 3264492	B2	20020311		
US 5716972	A	19980210	US 1994-256499	19941122
US 6008235	A	19991228	US 1997-995086	19971219
PRIORITY APPLN. INFO.:			US 1992-819552 A2	19920113
			WO 1993-US675 A	19930113
			US 1994-256499 A3	19941122

OTHER SOURCE(S): MARPAT 120:8592
GI



I

AB The title compds. I [R1 = mono- or disubstituted 4-quinolyl, 4-pyridyl, 1-imidazolyl, 1-benzimidazolyl, 4-pyrimidinyl; R2 = mono-

or disubstituted Ph; R3 = (X)r(Q)s(Y)t; Q = alkenyl, alkynyl, cycloalkyl, cycloalkenyl, heterocyclic, etc.; X = H, (un)substituted alkylene, (un)substituted NH, O, S, (O)m; m = 0-2; Y = H, C1-10 alkyl, halo-substituted C1-10 alkyl, halogen, etc.; r, s = 0,1; t = 0-3: R4 = H, C1-4 alkyl, C2-10 alkenyl, C2-10 alkynyl, C3-7 cycloalkyl, C5-7 cycloalkenyl, heterocyclic, etc.], which have cytokine suppressive and antiinflammatory properties and are capable of inhibiting cytokines such as IL-1, IL-6, IL-8, and tissue necrosis factor, are prepared and are useful in the **treatment** of cytokine-mediated diseases. Thus, I (R1 = 4-pyridyl, R2 = 4-FC6H4, R3 = Ph, R4 = H) (II) was prepared from phenylglycine in 5 steps and II demonstrated 50% inhibitory concentration for production of tissue necrosis factor by monocytes of 0.5-3.5 μM.

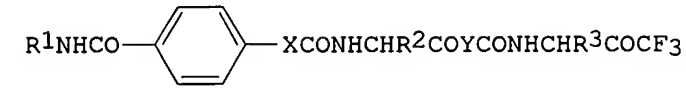
IT **151385-47-6P 151385-51-2P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and reaction of, in preparation of cytokine formation inhibitors)

L6 ANSWER 14 OF 19 CAPLUS COPYRIGHT 2006 ACS on STN
ED Entered STN: 28 Nov 1992
ACCESSION NUMBER: 1992:612979 CAPLUS
DOCUMENT NUMBER: 117:212979
TITLE: Preparation of trifluoromethylketone tripeptide derivatives as human leukocyte elastase inhibitors
INVENTOR(S): Hemmi, Keiji; Shima, Ichiro; Imai, Keisuke; Tanaka, Hirokazu
PATENT ASSIGNEE(S): Fujisawa Pharmaceutical Co., Ltd., Japan
SOURCE: Eur. Pat. Appl., 26 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 494071	A2	19920708	EP 1992-100014	19920102
EP 494071	A3	19930505		
EP 494071	B1	19970416		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, PT, SE				
US 5296591	A	19940322	US 1991-805610	19911212
FI 9105996	A	19920701	FI 1991-5996	19911219
FI 106379	B1	20010131		
AU 9189853	A1	19920702	AU 1991-89853	19911219
AU 641577	B2	19930923		
JP 04297446	A2	19921021	JP 1991-361134	19911219
JP 06099378	B4	19941207		
KR 192991	B1	19990615	KR 1991-24710	19911227
RU 2073684	C1	19970220	RU 1991-5010583	19911228
CA 2058560	AA	19920701	CA 1991-2058560	19911230
CA 2058560	C	20001212		
CN 1063108	A	19920729	CN 1991-112615	19911230
CN 1040003	B	19980930		
HU 60507	A2	19920928	HU 1991-4153	19911230
HU 210263	B	19950328		
ZA 9110200	A	19921028	ZA 1991-10200	19911230
NO 9200035	A	19920701	NO 1992-35	19920102

NO 309274	B1	20010108			
AT 151775	E	19970515	AT 1992-100014		19920102
ES 2099755	T3	19970601	ES 1992-100014		19920102
PRIORITY APPLN. INFO.:			GB 1990-28231	A	19901231
			GB 1991-19713	A	19910916

OTHER SOURCE(S): MARPAT 117:212979
GI



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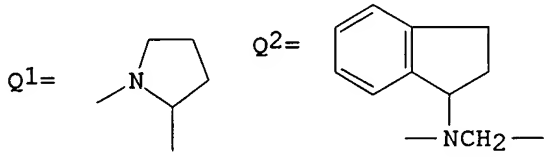

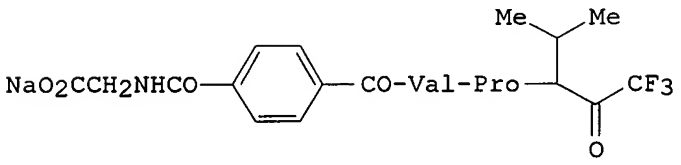

II

AB Title compds. [I; R1 = alkyl[substituted by 1-2 of (esterified) carboxy, dialkylcarbanoyl, (substituted) phenylalkyl], halophenyl, morpholino, morpholinoalkyl; R2, R3 = alkyl; X = null, NH; Y = Q1, Q2], were prepared Thus, II, prepared via hydrogenolysis of the benzyl ester followed by salification, at 200 μg/site intratracheally gave 97% inhibition of porcine pancreas elastase-induced emphysema in hamsters.

IT **144055-63-0P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of, as human leukocyte elastase inhibitor)

L6 ANSWER 15 OF 19 CAPLUS COPYRIGHT 2006 ACS on STN
ED Entered STN: 08 Aug 1992
ACCESSION NUMBER: 1992:448228 CAPLUS
DOCUMENT NUMBER: 117:48228
TITLE: Preparation of novel methotrexate derivatives as drugs
INVENTOR(S): Ohi, Nobuhiro; Matsuoka, Hiroharu; Miyamoto, Katsuhito; Suzuki, Hiroshi; Kato, Nobuaki; Tsuji, Keiichiro; Takeda, Yasuhisa; Mihara, Masahiko; Nishina, Hiromichi; et al.
PATENT ASSIGNEE(S): Chugai Pharmaceutical Co., Ltd., Japan
SOURCE: PCT Int. Appl., 93 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
WO 9203436	A1	19920305	WO 1991-JP1078		19910814
W: AT, AU, BB, BG, BR, CA, CH, DE, DK, ES, FI, GB, HU, KR, LK, LU, MC, MG, MW, NL, NO, PL, RO, SD, SE, SU, US					
RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, DE, DK, ES, FR, GA, GB, GN, GR, IT, LU, ML, MR, NL, SE, SN, TD, TG					
JP 04352785	A2	19921207	JP 1991-228158		19910530
JP 04368385	A2	19921221	JP 1991-247141		19910612
JP 05132485	A2	19930528	JP 1991-288243		19910813
JP 3124592	B2	20010115			
CA 2088665	AA	19920215	CA 1991-2088665		19910814
CA 2088665	C	20010501			
AU 9183332	A1	19920317	AU 1991-83332		19910814
CN 1059725	A	19920325	CN 1991-105803		19910814
CN 1032858	B	19960925			
ZA 9106419	A	19920729	ZA 1991-6419		19910814
EP 543997	A1	19930602	EP 1991-914615		19910814
EP 543997	B1	19991208			
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE					
HU 64974	A2	19940328	HU 1993-264		19910814
RU 2109016	C1	19980420	RU 1993-5141		19910814
AT 187455	E	19991215	AT 1991-914615		19910814
ES 2141710	T3	20000401	ES 1991-914615		19910814
JP 05202047	A2	19930810	JP 1992-214465		19920702
JP 3100469	B2	20001016			
JP 05194231	A2	19930803	JP 1992-237555		19920722
JP 3387943	B2	20030317			
US 5354753	A	19941011	US 1993-971773		19930212
GR 3032704	T3	20000630	GR 2000-400402		20000218
PRIORITY APPLN. INFO.:			JP 1990-214691	A	19900814
			JP 1990-215639	A	19900815
			JP 1990-253466	A	19900921
			JP 1990-293107	A	19901030
			JP 1990-331845	A	19901129
			JP 1991-180626	A	19910419
			JP 1991-185943	A	19910423
			JP 1991-228158	A	19910530
			JP 1991-247141	A	19910612
			JP 1991-258301	A	19910703
			JP 1991-279047	A	19910730
			WO 1991-JP1078	A	19910814

OTHER SOURCE(S): MARPAT 117:48228
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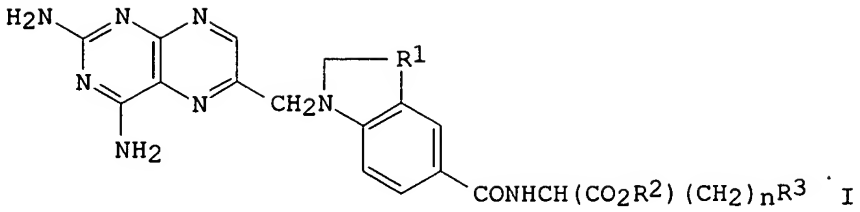

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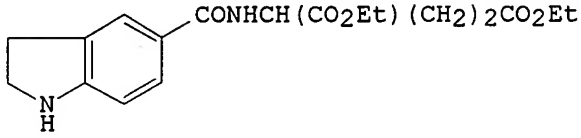

II

AB Methotrexate derivs. [I; R1 = CH2, CH2CH2, CH2O, CH2S, CH2SO; R2 = H, C1-4 alkyl, PhCH2; R3 = CO2R4, NHCOR5, CONR6R7 where in R4 = H, C1-4 alkyl; R5 = (substituted) Ph; R6 = H, C1-4 alkyl; R7 = C1-4 alkyl, (substituted) Ph, etc.; n = 1-4], useful as **antirheumatics**, anticancer agents, and in **treating** psoriasis, are prepared A mixture of 214 mg diester II (preparation given) and 250 mg 6-bromomethyl-2,4-diaminopteridine HBr-Me2CHOH in DMF was **treated** with Et3N to give 200 mg diester I (R1 = CH2, R2 = Et, R1 = CO2Et, n = 2), which (170 mg) was saponified to give 130 mg diacid I (R1 = CH2, R2 = H, R3 = CO2H, n = 2), which was effective in **treating** rheumatism, psoriasis, and mouse lymphoid neoplasm P-388, and colon-26 carcinoma.

IT **142165-64-8P 142165-65-9P 142165-66-0P 142166-10-7P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and reaction of, in preparation of methotrexate derivative)

IT **142166-12-9P 142166-32-3P 142166-34-5P**
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of, as drug)

L6 ANSWER 16 OF 19 CAPLUS COPYRIGHT 2006 ACS on STN
ED Entered STN: 17 Feb 1990
ACCESSION NUMBER: 1990:56690 CAPLUS
DOCUMENT NUMBER: 112:56690
TITLE: Preparation and testing of N-[(aminopyrimidinyl)acyl]glutamates as neoplasm inhibitors
INVENTOR(S): Taylor, Edward C.; Harrington, Philip M.; Shih, Chuan
PATENT ASSIGNEE(S): Princeton University, USA; Eli Lilly and Co.
SOURCE: Eur. Pat. Appl., 9 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 325343	A2	19890726	EP 1989-300045	19890105
EP 325343	A3	19900905		

EP 325343	B1	19940622			
R: AT, BE, CH, DE, ES, FR, GB, GR, IT, LI, LU, NL, SE					
US 4871743	A	19891003	US 1988-144970		19880119
ES 2055024	T3	19940816	ES 1989-300045		19890105
CA 1314547	A1	19930316	CA 1989-588039		19890112
JP 02000781	A2	19900105	JP 1989-10979		19890119
PRIORITY APPLN. INFO.:			US 1988-144970	A	19880119

OTHER SOURCE(S): CASREACT 112:56690; MARPAT 112:56690
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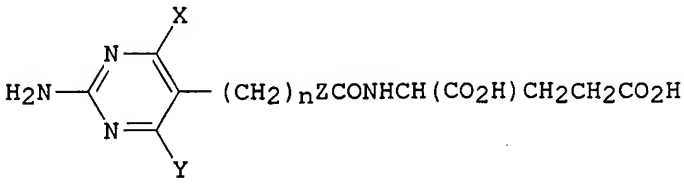

I

AB The title compds. [I; X, Y = OH, amino; Z = (F- or Cl-substituted) 1,4-phenylene, cyclohexa-1,4-diyl, C2-5 alkylene; n = 2-6], useful as neoplasm inhibitors and for **treating** mycosis fungoides, psoriasis, and arthritis, were prepared Thus, guanidine and Me 4-(5-carboethoxy-5-cyanopentyl)benzoate (preparation given) were stirred 12 h in DMF with gentle heating to give Me 4-[4-(2,4-diamino-6-hydroxypyrimidin-5-yl)butyl]benzoate, which was stirred 18 h in 1N NaOH with gentle heating followed by acidification with HOAc to give the free acid. The latter was stirred with N-methylmorpholine and Ph N-phenylphosphoramidochloridate in N-methylpyrrolidone for 1 h followed by addition of di-Et L-glutamate hydrochloride and stirring for 24 h. The coupling product was hydrolyzed by stirring in 1N hydroxide for 72 h followed by acidification with HCl to give L-I (X = OH, Y = NH2, Z = 1,4-phenylene, n = 4) (II). II had an IC50 of 0.0632 μ/gmL against CCRF-CEM cells. I may be administered at higher doses than methotrexate.

IT **124656-59-3P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of, as intermediate for neoplasm inhibitor)

L6 ANSWER 17 OF 19 CAPLUS COPYRIGHT 2006 ACS on STN
ED Entered STN: 12 May 1984
ACCESSION NUMBER: 1980:181659 CAPLUS
DOCUMENT NUMBER: 92:181659
TITLE: Cysteine derivatives
INVENTOR(S): Yuki, Hiroshi; Shiraki, Masami; Naka, Yoichi; Maruyama, Hiroshi
PATENT ASSIGNEE(S): Yoshitomi Pharmaceutical Industries, Ltd., Japan
SOURCE: Jpn. Kokai Tokkyo Koho, 11 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 54141726	A2	19791105	JP 1978-47416	19780420

PRIORITY APPLN. INFO.: JP 1978-47416 A 19780420

AB Twenty-seven RR1NZNHC(:Z1)SZ2CH(NHR3)CO2R2 [I; R, R1 = alkyl, aralkyl; RR1N may form a ring; R2 = H, alkyl; R3 = H, R4CO (R4 = alkyl, alkenyl, aryl, etc), R5SO2 (R5 = alkyl, aryl); Z = alkylene; Z1 = S, O; Z2 = CH2, CH2CH2, CHR6 (R6 = alkyl, aryl)] and their acid salts were prepared by the reaction of HSZ2CH(NHR3)CO2R2 with RR1NZNCS. Data of some of I were given as to leukocytopenia inhibition and adjuvant anti-arthritis in male rats. Thus, a mixture of 10 g L-cysteine-HCl, 6 mL pyridine, and 9.4 g Me2NCH2CH2NCS in CHCl3 was stirred 5 h at 50-60° to give L-Me2NCH2CH2NHC(S)SCH2CH(NH2)CO2H.HCl.

IT **73444-80-1P 73444-85-6P 73444-87-8P**
73444-88-9P 73444-92-5P 73445-10-0P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)

L6 ANSWER 18 OF 19 CAPLUS COPYRIGHT 2006 ACS on STN
ED Entered STN: 12 May 1984
ACCESSION NUMBER: 1980:58799 CAPLUS
DOCUMENT NUMBER: 92:58799
TITLE: Penicillamine derivatives
INVENTOR(S): Shiraki, Masami; Maruyama, Yutaka; Goto, Ichiyo
PATENT ASSIGNEE(S): Yoshitomi Pharmaceutical Industries, Ltd., Japan
SOURCE: Jpn. Kokai Tokkyo Koho, 8 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 54098782	A2	19790803	JP 1978-3933	19780117
PRIORITY APPLN. INFO.:			JP 1978-3933	19780117

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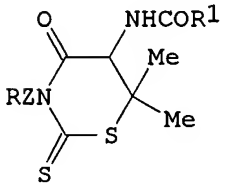


I

AB Penicillamine derivs. I [R = H, alkyl, aryl, aromatic heterocyclyl, R2R3N; R2, R3 = alkyl or NR2R3 = heterocyclyl; R1 = R4SO2NH (R4 = alkyl, CF3, alkyl- or haloaryl, aryl possessing alkanoyl or AcO, aromatic heterocyclyl, aromatic heterocyclyl alkyl, aryloxyalkyl, α-methylbenzyl; Z = C1-5 alkylene] were prepared by **treating** HSCMe2CH(NHOR1)C12R5 (II) (R5 = H, alkyl) with isothiocyanates RZNCS (III), or by eliminating R5OH from RZNHC(:S)SCMe2CH(NHCOR1)CO2R5 IV. I have antiinflammatory, **antirheumatic**, immunosuppressant , analgesic, antibacterial,

and antitumor activity. Thus, stirring 30.3 g D-penicillamine Et ester HCl salt in water and AcOEt, with NaHCO3 and 34 g p-MeSO2NHC6H4COCl 30 min at < 10°, and 3 h at room temperature gave 52 g II (R1 = MeSO2NHC6H4; R4 = Me; R5 = Et), which in pyridine was stirred with 21 g III (R = R2R3N; R2, R3 = Me; A = C2H4) 1.5 h at room temperature and 6 h at 65-70° to give 48 g corresponding I. Similarly prepared were I (R, A, R1 given): Me2N, C2H4, 2-furoyl; Ph, CH2, PhOCH2; Me2N, C2H4, hydroatropoly.

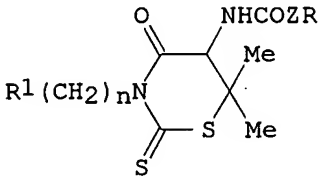
IT **67749-32-0P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and reaction with isothiocyanates)

L6 ANSWER 19 OF 19 CAPLUS COPYRIGHT 2006 ACS on STN
ED Entered STN: 12 May 1984
ACCESSION NUMBER: 1978:563589 CAPLUS
DOCUMENT NUMBER: 89:163589
TITLE: Penicillamine compounds
INVENTOR(S): Shiroki, Masami; Maruyama, Yutaka; Goto, Kazuhiro
PATENT ASSIGNEE(S): Yoshitomi Pharmaceutical Industries, Ltd., Japan
SOURCE: Ger. Offen., 29 pp.
CODEN: GWXXBX
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 2800488	A1	19780713	DE 1978-2800488	19780105
JP 53087369	A2	19780801	JP 1977-1008	19770108
FR 2379530	A1	19780901	FR 1977-39743	19771230
FR 2379530	B1	19820702		
GB 1554541	A	19791024	GB 1978-4	19780103
SE 7800162	A	19780709	SE 1978-162	19780105
AT 7800078	A	19800315	AT 1978-78	19780105
AT 359077	B	19801027		
CA 1094064	A1	19810120	CA 1978-294355	19780105
BE 862725	A1	19780502	BE 1978-184176	19780106
NL 7800175	A	19780711	NL 1978-175	19780106
US 4169899	A	19791002	US 1978-867413	19780106

PRIORITY APPLN. INFO.: JP 1977-1008 A 19770108

OTHER SOURCE(S): MARPAT 89:163589
GI



I

AB The title compds. I (R = alkyl, aryl, aryloxy, heterocyclyl; R1 = H, aliphatic group, carbalkoxy, aryl, cyclic or acyclic substituted amino; Z = O, direct bond, alkylene, alkenylene; n = 1-15) were prepared for use

as antiinflammatory and **antirheumatic** agents (test data tabulated). Thus, D-N-benzoylpenicillamine Me ester was **treated** with Et2NCH2CH2NCS in pyridine to give I (RZ = Ph, R1 = Et2N, n = 2). I are interconvertible with R1(CH2)nNHCS2CMe2CH(CO2H)NHCOZR or their esters.

IT **67749-32-0P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and reaction of, with alkyl isothiocyanates)

IT **67749-34-2 67749-35-3**
RL: RCT (Reactant); RACT (Reactant or reagent)
(reaction of, with alkyl isothiocyanates)

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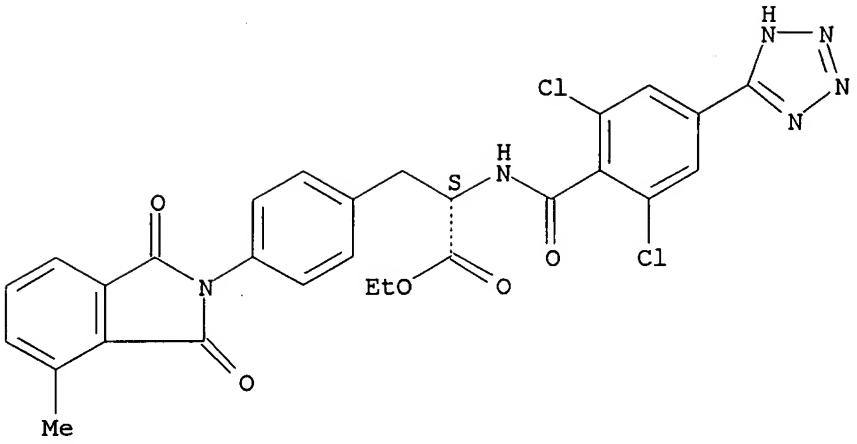
L7 72 SEA FILE=REGISTRY ABB=ON PLU=ON (142165-64-8/BI OR 142165-65-9/BI OR 142166-12-9/BI OR 142166-10-7/BI OR 142166-32-3/BI OR 142166-34-5/BI OR 67749-32-0/BI OR 124656-59-3/BI OR 126632-37-9/BI OR 126632-47-1/BI OR 13726-52-8/BI OR 142165-66-0/BI OR 144055-63-0/BI OR 146464-94-0/BI OR 151385-47-6/BI OR 151385-51-2/BI OR 153304-23-5/BI OR 153304-25-7/BI OR 153304-32-6/BI OR 153304-41-7/BI OR 153304-47-3/BI OR 153304-48-4/BI OR 153304-51-9/BI OR 153304-62-2/BI OR 153304-63-3/BI OR 153802-63-2/BI OR 153802-68-7/BI OR 156578-93-7/BI OR 162368-25-4/BI OR 171905-67-2/BI OR 186810-07-1/BI OR 199674-64-1/BI OR 199674-74-3/BI OR 215105-57-0/BI OR 232274-09-8/BI OR 232274-27-0/BI OR 232274-28-1/BI OR 232274-31-6/BI OR 232275-24-0/BI OR 232275-26-2/BI OR 232276-71-0/BI OR 232276-72-1/BI OR 241498-60-2/BI OR 402567-05-9/BI OR 402567-08-2/BI OR 402567-10-6/BI OR 402567-12-8/BI OR 402567-14-0/BI OR 402567-17-3/BI OR 402567-19-5/BI OR 402567-20-8/BI OR 402567-23-1/BI OR 402567-26-4/BI OR 402567-28-6/BI OR 402567-29-7/BI OR 402567-40-2/BI OR 402567-45-7/BI OR 402567-46-8/BI OR 402567-48-0/BI OR 402567-49-1/BI OR 402567-50-4/BI OR 402567-53-7/BI OR 409127-28-2/BI OR 409127-29-3/BI OR 67749-34-2/BI OR 67749-35-3/BI OR 73444-80-1/BI OR 73444-85-6/BI OR 73444-87-8/BI OR 73444-88-9/BI OR 73444-92-5/BI OR 73445-10-0/BI)

Random Strs/ RNs displayed ↓

=> d 1,3,22,23,25,27,31,32,34-38,40,49-53,57,60,62,63,64,69,72 ide can

L7 ANSWER 1 OF 72 REGISTRY COPYRIGHT 2006 ACS on STN
RN **409127-29-3** REGISTRY
ED Entered STN: 30 Apr 2002
CN L-Phenylalanine, N-[2,6-dichloro-4-(1H-tetrazol-5-yl)benzoyl]-4-(1,3-dihydro-4-methyl-1,3-dioxo-2H-isoindol-2-yl)-, ethyl ester (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C28 H22 Cl2 N6 O5
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER, USPATFULL

Absolute stereochemistry.



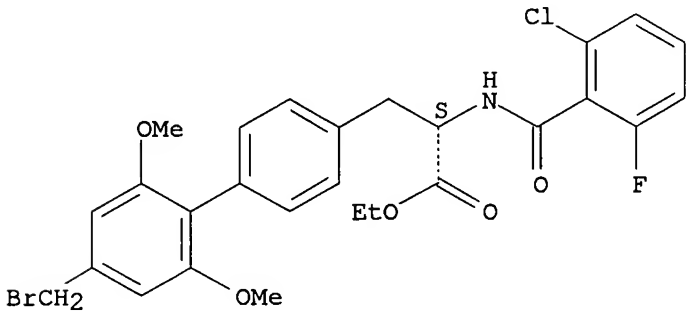
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 136:310177

L7 ANSWER 3 OF 72 REGISTRY COPYRIGHT 2006 ACS on STN
RN **402567-53-7** REGISTRY
ED Entered STN: 22 Mar 2002
CN [1,1'-Biphenyl]-4-propanoic acid, 4'-(bromomethyl)-α-[(2-chloro-6-fluorobenzoyl)amino]-2',6'-dimethoxy-, ethyl ester, (αS)-(9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C27 H26 Br Cl F N O5
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER, USPATFULL

Absolute stereochemistry.



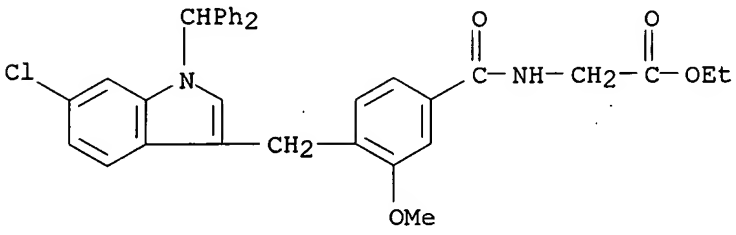
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

2 REFERENCES IN FILE CA (1907 TO DATE)
2 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 139:358808

REFERENCE 2: 136:217048

L7 ANSWER 22 OF 72 REGISTRY COPYRIGHT 2006 ACS on STN
RN **241498-60-2** REGISTRY
ED Entered STN: 25 Sep 1999
CN Glycine, N-[4-[[6-chloro-1-(diphenylmethyl)-1H-indol-3-yl]methyl]-3-methoxybenzoyl]-, ethyl ester (9CI) (CA INDEX NAME)
MF C34 H31 Cl N2 O4
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER, USPATFULL



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

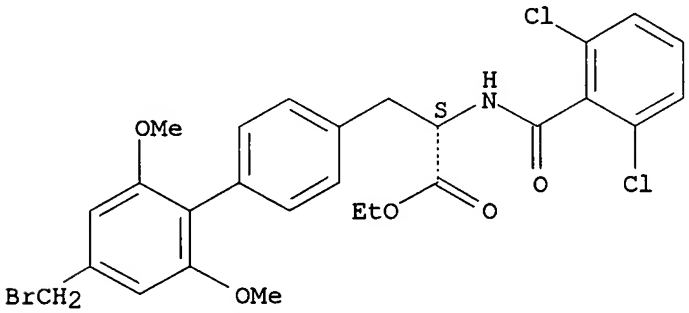
2 REFERENCES IN FILE CA (1907 TO DATE)
2 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 138:55866

REFERENCE 2: 131:199619

L7 ANSWER 23 OF 72 REGISTRY COPYRIGHT 2006 ACS on STN
RN **232276-72-1** REGISTRY
ED Entered STN: 13 Aug 1999
CN [1,1'-Biphenyl]-4-propanoic acid, 4'-(bromomethyl)-α-[(2,6-dichlorobenzoyl)amino]-2',6'-dimethoxy-, ethyl ester, (αS)-(9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C27 H26 Br Cl2 N O5
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER, USPAT2, USPATFULL

Absolute stereochemistry.



Searcher : Shears 571-272-2528

PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

3 REFERENCES IN FILE CA (1907 TO DATE)
3 REFERENCES IN FILE CAPLUS (1907 TO DATE)

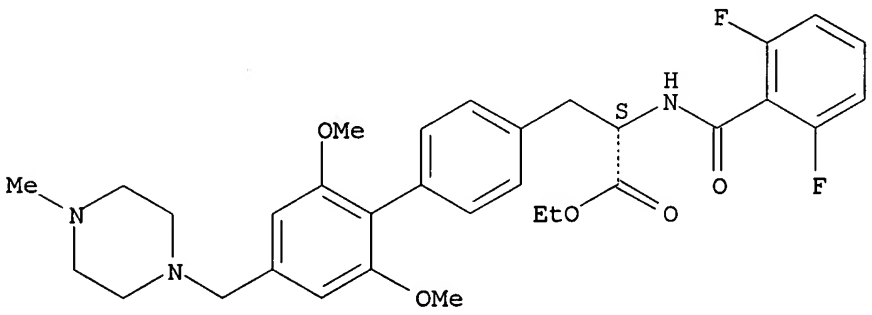
REFERENCE 1: 139:358808

REFERENCE 2: 136:217048

REFERENCE 3: 131:116517

L7 ANSWER 25 OF 72 REGISTRY COPYRIGHT 2006 ACS on STN
RN **232275-26-2** REGISTRY
ED Entered STN: 13 Aug 1999
CN [1,1'-Biphenyl]-4-propanoic acid, α-[(2,6-difluorobenzoyl)amino]-2',6'-dimethoxy-4'-[(4-methyl-1-piperazinyl)methyl]-, ethyl ester, dihydrochloride, (αS)- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C32 H37 F2 N3 O5 . 2 Cl H
SR CA
LC STN Files: CA, CAPLUS, USPAT2, USPATFULL
CRN (776280-40-1)

Absolute stereochemistry.



●2 HCl

2 REFERENCES IN FILE CA (1907 TO DATE)
2 REFERENCES IN FILE CAPLUS (1907 TO DATE)

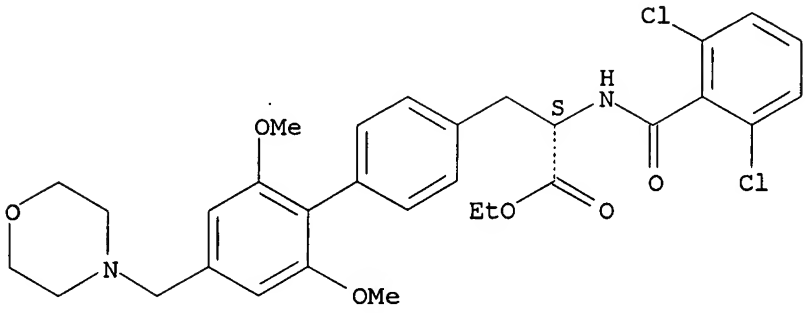
REFERENCE 1: 134:275760

REFERENCE 2: 131:116517

L7 ANSWER 27 OF 72 REGISTRY COPYRIGHT 2006 ACS on STN
RN **232274-31-6** REGISTRY
ED Entered STN: 13 Aug 1999
CN [1,1'-Biphenyl]-4-propanoic acid, α-[(2,6-dichlorobenzoyl)amino]-2',6'-dimethoxy-4'-(4-morpholinylmethyl)-, ethyl ester, monohydrochloride, (αS)- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C31 H34 Cl2 N2 O6 . Cl H
SR CA

LC STN Files: CA, CAPLUS, USPAT2, USPATFULL
CRN (697735-96-9)

Absolute stereochemistry.



● HCl

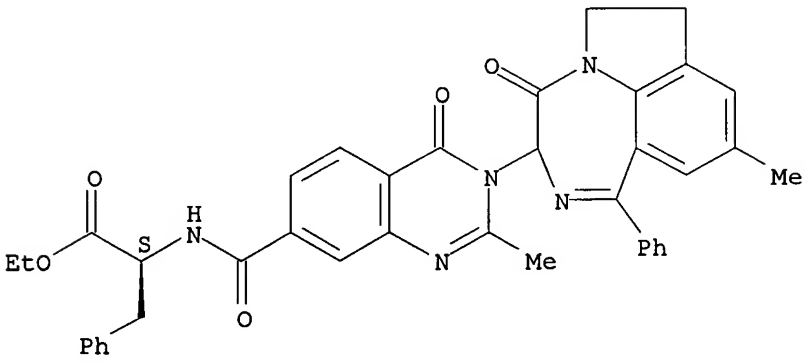
2 REFERENCES IN FILE CA (1907 TO DATE)
2 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 134:275760

REFERENCE 2: 131:116517

L7 ANSWER 31 OF 72 REGISTRY COPYRIGHT 2006 ACS on STN
RN **215105-57-0** REGISTRY
ED Entered STN: 03 Dec 1998
CN L-Phenylalanine, N-[[3,4-dihydro-2-methyl-4-oxo-3-(3,4,6,7-tetrahydro-9-methyl-4-oxo-1-phenylpyrrolo[3,2,1-jk][1,4]benzodiazepin-3-yl)-7-quinazolinyl]carbonyl]-, ethyl ester (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C39 H35 N5 O5
SR CA
LC STN Files: CA, CAPLUS, USPATFULL

Absolute stereochemistry.

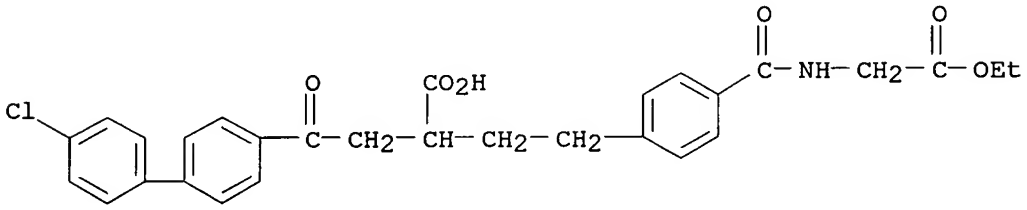


PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 129:330743

L7 ANSWER 32 OF 72 REGISTRY COPYRIGHT 2006 ACS on STN
RN **199674-74-3** REGISTRY
ED Entered STN: 13 Jan 1998
CN [1,1'-Biphenyl]-4-butanoic acid, 4'-chloro-α-[2-[4-[[(2-ethoxy-2-oxoethyl)amino]carbonyl]phenyl]ethyl]-γ-oxo- (9CI) (CA INDEX NAME)
FS 3D CONCORD
MF C29 H28 Cl N O6
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER, USPATFULL



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

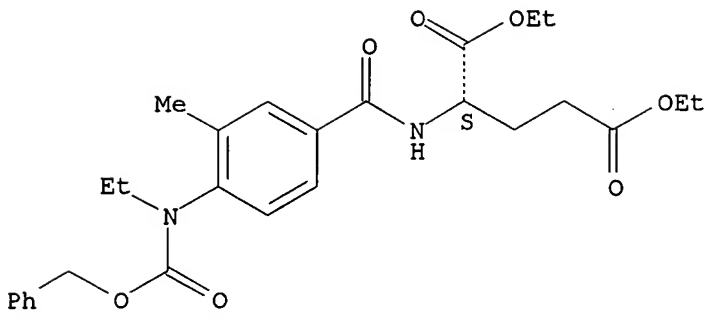
2 REFERENCES IN FILE CA (1907 TO DATE)
2 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 129:230536

REFERENCE 2: 128:34585

L7 ANSWER 34 OF 72 REGISTRY COPYRIGHT 2006 ACS on STN
RN **186810-07-1** REGISTRY
ED Entered STN: 07 Mar 1997
CN L-Glutamic acid, N-[4-[ethyl[(phenylmethoxy)carbonyl]amino]-3-methylbenzoyl]-, diethyl ester (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C27 H34 N2 O7
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER

Absolute stereochemistry.



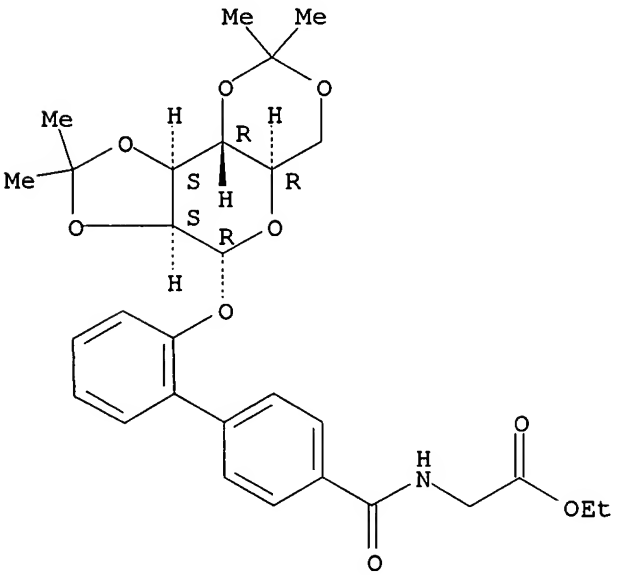
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 126:157483

L7 ANSWER 35 OF 72 REGISTRY COPYRIGHT 2006 ACS on STN
RN **171905-67-2** REGISTRY
ED Entered STN: 05 Jan 1996
CN Glycine, N-[[2'-[[2,3:4,6-bis-O-(1-methylethylidene)-α-D-mannopyranosyl]oxy][1,1'-biphenyl]-4-yl]carbonyl]-, ethyl ester (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C29 H35 N O9
SR CA
LC STN Files: CA, CAPLUS, USPATFULL

Absolute stereochemistry.



Searcher : Shears 571-272-2528

PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

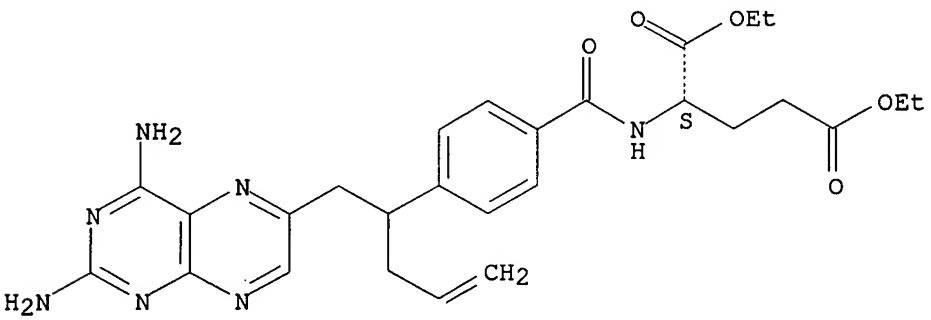
2 REFERENCES IN FILE CA (1907 TO DATE)
2 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 124:146671

REFERENCE 2: 124:56563

L7 ANSWER 36 OF 72 REGISTRY COPYRIGHT 2006 ACS on STN
RN **162368-25-4** REGISTRY
ED Entered STN: 21 Apr 1995
CN L-Glutamic acid, N-[4-[1-[(2,4-diamino-6-pteridinyl)methyl]-3-butenyl]benzoyl]-, diethyl ester (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C27 H33 N7 O5
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER, USPATFULL

Absolute stereochemistry.



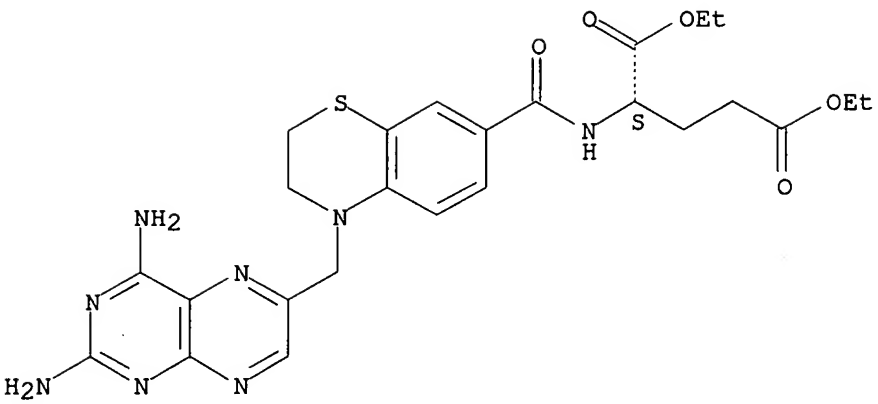
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 122:240437

L7 ANSWER 37 OF 72 REGISTRY COPYRIGHT 2006 ACS on STN
RN **156578-93-7** REGISTRY
ED Entered STN: 26 Jul 1994
CN L-Glutamic acid, N-[[4-[(2,4-diamino-6-pteridinyl)methyl]-3,4-dihydro-2H-1,4-benzothiazin-7-yl]carbonyl]-, diethyl ester (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN 2H-1,4-Benzothiazine, L-glutamic acid deriv.
FS STEREOSEARCH
MF C25 H30 N8 O5 S
SR CA
LC STN Files: CA, CAPLUS

Absolute stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

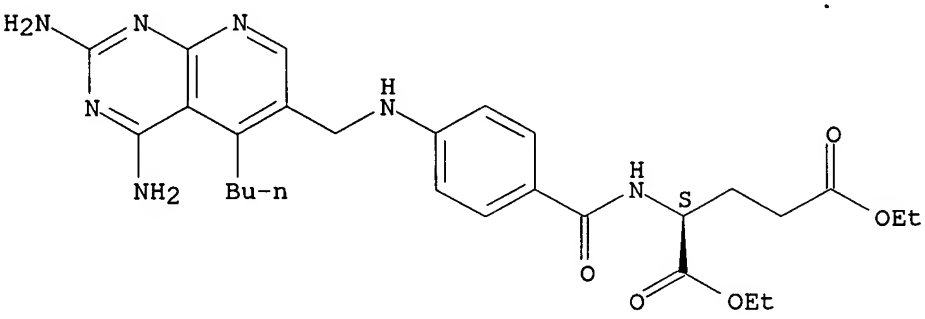
2 REFERENCES IN FILE CA (1907 TO DATE)
2 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 126:84069

REFERENCE 2: 121:99796

L7 ANSWER 38 OF 72 REGISTRY COPYRIGHT 2006 ACS on STN
RN **153802-68-7** REGISTRY
ED Entered STN: 23 Mar 1994
CN L-Glutamic acid, N-[4-[[(2,4-diamino-5-butylpyrido[2,3-d]pyrimidin-6-yl)methyl]amino]benzoyl]-, diethyl ester (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN Pyrido[2,3-d]pyrimidine, L-glutamic acid deriv.
FS STEREOSEARCH
MF C28 H37 N7 O5
SR CA
LC STN Files: CA, CAPLUS, CASREACT, TOXCENTER, USPATFULL

Absolute stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

3 REFERENCES IN FILE CA (1907 TO DATE)
3 REFERENCES IN FILE CAPLUS (1907 TO DATE)

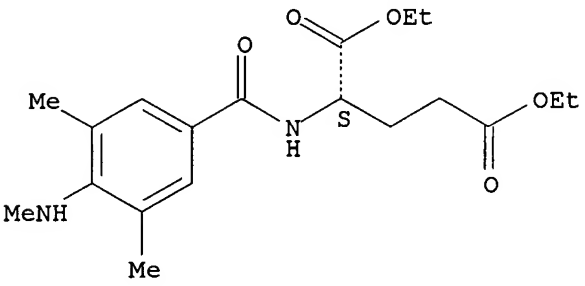
REFERENCE 1: 125:196375

REFERENCE 2: 124:9376

REFERENCE 3: 120:270438

L7 ANSWER 40 OF 72 REGISTRY COPYRIGHT 2006 ACS on STN
RN **153304-63-3** REGISTRY
ED Entered STN: 25 Feb 1994
CN L-Glutamic acid, N-[3,5-dimethyl-4-(methylamino)benzoyl]-, diethyl ester (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C19 H28 N2 O5
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER, USPATFULL

Absolute stereochemistry.



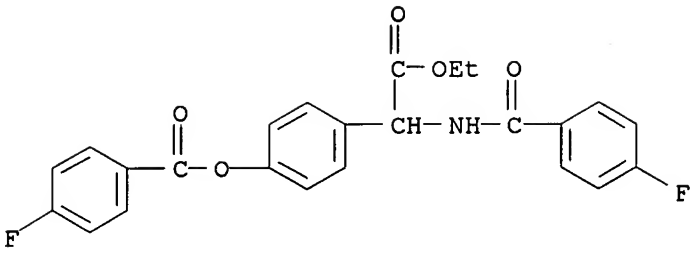
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

2 REFERENCES IN FILE CA (1907 TO DATE)
2 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 126:157483

REFERENCE 2: 120:164208

L7 ANSWER 49 OF 72 REGISTRY COPYRIGHT 2006 ACS on STN
RN **151385-51-2** REGISTRY
ED Entered STN: 23 Nov 1993
CN Benzeneacetic acid, α-[(4-fluorobenzoyl)amino]-4-[(4-fluorobenzoyl)oxy]-, ethyl ester (9CI) (CA INDEX NAME)
FS 3D CONCORD
MF C24 H19 F2 N O5
SR CA
LC STN Files: CA, CAPLUS, USPATFULL

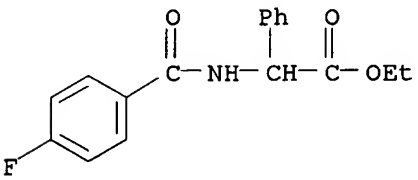


PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 120:8592

L7 ANSWER 50 OF 72 REGISTRY COPYRIGHT 2006 ACS on STN
RN **151385-47-6** REGISTRY
ED Entered STN: 23 Nov 1993
CN Benzeneacetic acid, α-[(4-fluorobenzoyl)amino]-, ethyl ester (9CI) (CA INDEX NAME)
FS 3D CONCORD
MF C17 H16 F N O3
SR CA
LC STN Files: CA, CAPLUS, USPATFULL



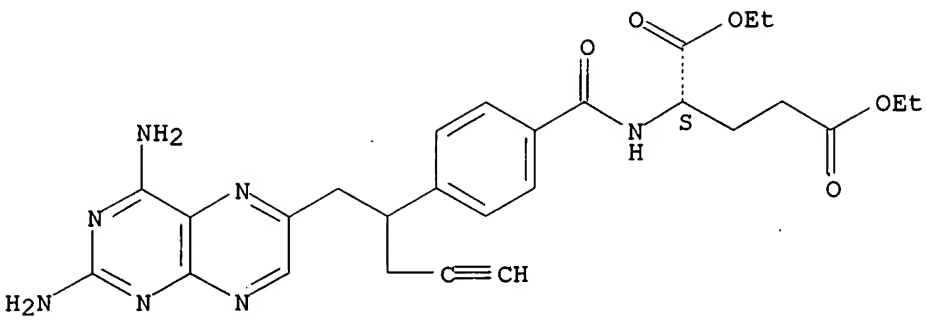
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 120:8592

L7 ANSWER 51 OF 72 REGISTRY COPYRIGHT 2006 ACS on STN
RN **146464-94-0** REGISTRY
ED Entered STN: 16 Mar 1993
CN L-Glutamic acid, N-[4-[1-[(2,4-diamino-6-pteridinyl)methyl]-3-butynyl]benzoyl]-, diethyl ester (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C27 H31 N7 O5
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER, USPATFULL

Absolute stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

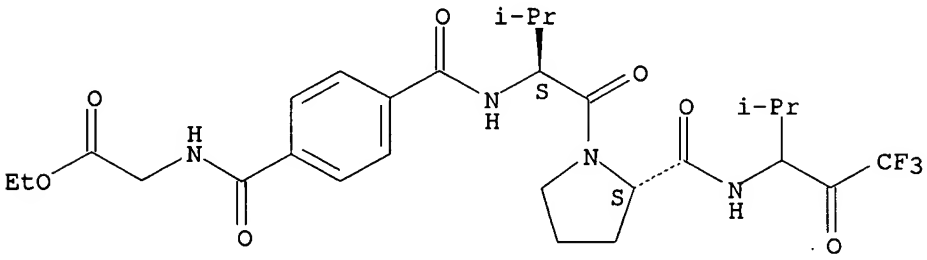
2 REFERENCES IN FILE CA (1907 TO DATE)
2 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 122:240437

REFERENCE 2: 119:72415

L7 ANSWER 52 OF 72 REGISTRY COPYRIGHT 2006 ACS on STN
RN **144055-63-0** REGISTRY
ED Entered STN: 21 Oct 1992
CN L-Prolinamide, N-[4-[[(2-ethoxy-2-oxoethyl)amino]carbonyl]benzoyl]-L-valyl-N-[3,3,3-trifluoro-1-(1-methylethyl)-2-oxopropyl]- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C28 H37 F3 N4 O7
SR CA
LC STN Files: CA, CAPLUS, USPATFULL

Absolute stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

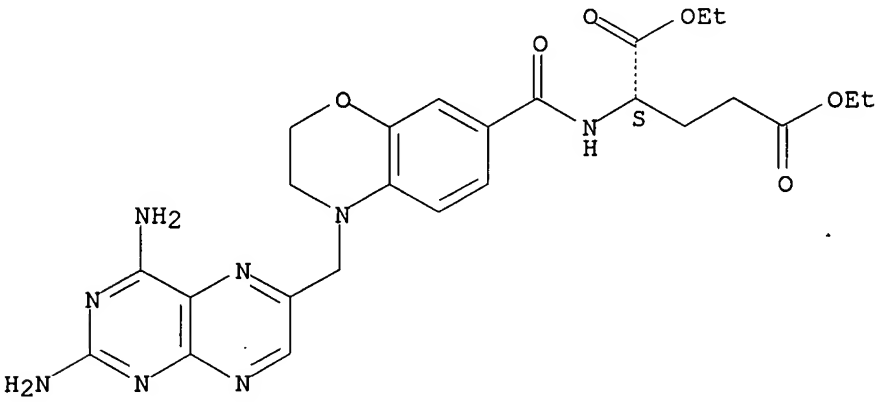
1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 117:212979

L7 ANSWER 53 OF 72 REGISTRY COPYRIGHT 2006 ACS on STN
RN **142166-34-5** REGISTRY
ED Entered STN: 01 Jul 1992
CN L-Glutamic acid, N-[[4-[(2,4-diamino-6-pteridinyl)methyl]-3,4-dihydro-

2H-1,4-benzoxazin-7-yl]carbonyl]-, diethyl ester (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN 2H-1,4-Benzoxazine, L-glutamic acid deriv.
FS STEREOSEARCH
MF C25 H30 N8 O6
SR CA
LC STN Files: CA, CAPLUS, CASREACT, TOXCENTER, USPATFULL

Absolute stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

3 REFERENCES IN FILE CA (1907 TO DATE)
3 REFERENCES IN FILE CAPLUS (1907 TO DATE)

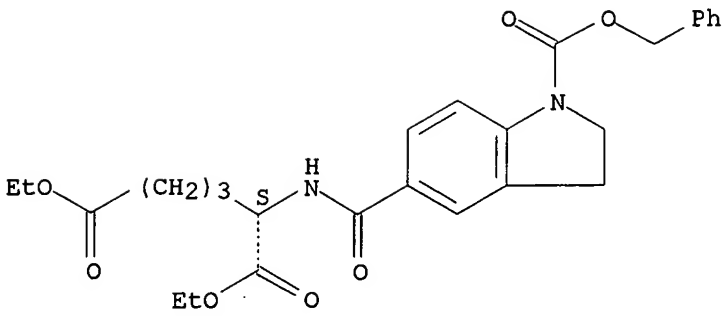
REFERENCE 1: 126:84069

REFERENCE 2: 121:99796

REFERENCE 3: 117:48228

L7 ANSWER 57 OF 72 REGISTRY COPYRIGHT 2006 ACS on STN
RN **142165-66-0** REGISTRY
ED Entered STN: 01 Jul 1992
CN Hexanedioic acid, 2-[[[2,3-dihydro-1-[(phenylmethoxy)carbonyl]-1H-indol-5-yl]carbonyl]amino]-, diethyl ester, (S)- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C27 H32 N2 O7
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER, USPATFULL

Absolute stereochemistry.



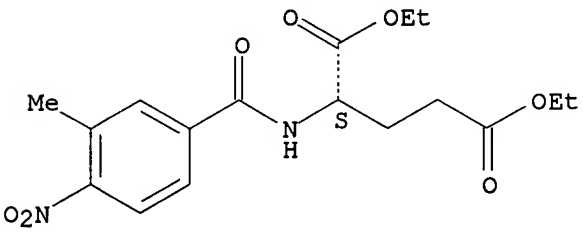
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 117:48228

L7 ANSWER 60 OF 72 REGISTRY COPYRIGHT 2006 ACS on STN
RN **126632-47-1** REGISTRY
ED Entered STN: 20 Apr 1990
CN L-Glutamic acid, N-(3-methyl-4-nitrobenzoyl)-, diethyl ester (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C17 H22 N2 O7
SR CA
LC STN Files: BEILSTEIN*, CA, CAPLUS, TOXCENTER, USPATFULL
(*File contains numerically searchable property data)

Absolute stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

5 REFERENCES IN FILE CA (1907 TO DATE)
5 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 126:157483

REFERENCE 2: 120:164208

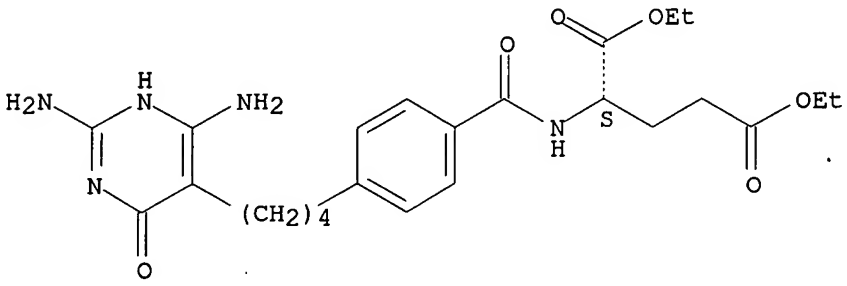
REFERENCE 3: 116:194810

REFERENCE 4: 112:179883

REFERENCE 5: 48:71803

L7 ANSWER 62 OF 72 REGISTRY COPYRIGHT 2006 ACS on STN
RN **124656-59-3** REGISTRY
ED Entered STN: 12 Jan 1990
CN L-Glutamic acid, N-[4-[4-(2,6-diamino-1,4-dihydro-4-oxo-5-pyrimidinyl)butyl]benzoyl]-, diethyl ester (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C24 H33 N5 O6
SR CA
LC STN Files: BEILSTEIN*, CA, CAPLUS, CASREACT, TOXCENTER, USPATFULL
(*File contains numerically searchable property data)

Absolute stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

2 REFERENCES IN FILE CA (1907 TO DATE)
2 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 112:99168

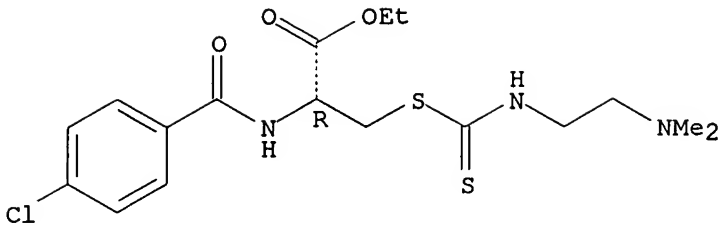
REFERENCE 2: 112:56690

L7 ANSWER 63 OF 72 REGISTRY COPYRIGHT 2006 ACS on STN
RN **73445-10-0** REGISTRY
ED Entered STN: 16 Nov 1984
CN L-Cysteine, N-(4-chlorobenzoyl)-, ethyl ester, [2-(dimethylamino)ethyl]carbamodithioate (ester), ethanedioate (salt) (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C17 H24 Cl N3 O3 S2 . x C2 H2 O4
LC STN Files: CA, CAPLUS

CM 1

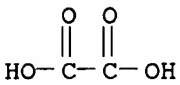
CRN 73444-86-7
CMF C17 H24 Cl N3 O3 S2

Absolute stereochemistry.



CM 2

CRN 144-62-7
CMF C2 H2 O4

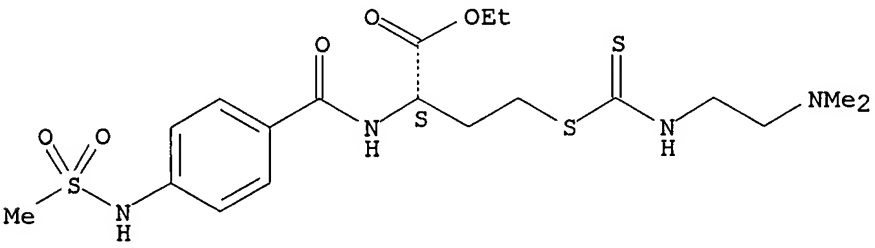


1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 92:181659

L7 ANSWER 64 OF 72 REGISTRY COPYRIGHT 2006 ACS on STN
RN **73444-92-5** REGISTRY
ED Entered STN: 16 Nov 1984
CN L-Homocysteine, N-[4-[(methylsulfonyl)amino]benzoyl]-, ethyl ester, [2-(dimethylamino)ethyl]carbamodithioate (ester) (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C19 H30 N4 O5 S3
LC STN Files: CA, CAPLUS

Absolute stereochemistry.



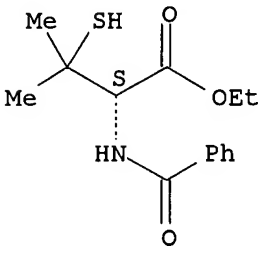
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 92:181659

L7 ANSWER 69 OF 72 REGISTRY COPYRIGHT 2006 ACS on STN
RN **67749-35-3** REGISTRY
ED Entered STN: 16 Nov 1984
CN D-Valine, N-benzoyl-3-mercapto-, ethyl ester (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C14 H19 N O3 S
LC STN Files: CA, CAPLUS, IFICDB, IFIPAT, IFIUDB, TOXCENTER, USPATFULL

Absolute stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

3 REFERENCES IN FILE CA (1907 TO DATE)
3 REFERENCES IN FILE CAPLUS (1907 TO DATE)

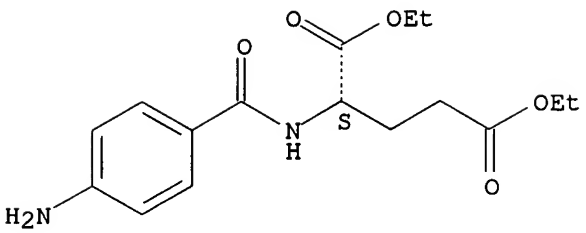
REFERENCE 1: 92:22517

REFERENCE 2: 91:57031

REFERENCE 3: 89:163589

L7 ANSWER 72 OF 72 REGISTRY COPYRIGHT 2006 ACS on STN
RN **13726-52-8** REGISTRY
ED Entered STN: 16 Nov 1984
CN L-Glutamic acid, N-(4-aminobenzoyl)-, diethyl ester (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN Glutamic acid, N-(p-aminobenzoyl)-, diethyl ester (6CI, 7CI)
CN Glutamic acid, N-(p-aminobenzoyl)-, diethyl ester, L- (8CI)
OTHER NAMES:
CN 4-Aminobenzoyl-L-glutamic acid, diethyl ester
CN Diethyl p-aminobenzoyl-L-glutamate
CN N-(4-Aminobenzoyl)-L-glutamic acid diethyl ester
CN NSC 82885
FS STEREOSEARCH
DR 51934-20-4, 90791-08-5, 34136-22-6, 194423-81-9
MF C16 H22 N2 O5
LC STN Files: BEILSTEIN*, CA, CAOLD, CAPLUS, CASREACT, CHEMCATS, CHEMINFORMRX, CHEMLIST, CSCHEM, SYNTHLINE, TOXCENTER, USPAT2, USPATFULL
(*File contains numerically searchable property data)
Other Sources: EINECS**
(**Enter CHEMLIST File for up-to-date regulatory information)

Absolute stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

96 REFERENCES IN FILE CA (1907 TO DATE)
96 REFERENCES IN FILE CAPLUS (1907 TO DATE)
4 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

REFERENCE 1: 144:128931

REFERENCE 2: 142:74804

REFERENCE 3: 141:313986

REFERENCE 4: 140:210038

REFERENCE 5: 140:111372

REFERENCE 6: 135:92600

REFERENCE 7: 133:120590

REFERENCE 8: 132:251049

REFERENCE 9: 131:359712

REFERENCE 10: 131:243279

FILE 'CAOLD' ENTERED AT 10:31:40 ON 21 MAR 2006

FILE COVERS 1907-1966
FILE LAST UPDATED: 01 May 1997 (19970501/UP)

This file contains CAS Registry Numbers for easy and accurate substance identification. Title keywords, authors, patent assignees, and patent information, e.g., patent numbers, are now searchable from 1907-1966. TIFF images of CA abstracts printed between 1907-1966 are available in the PAGE display formats.

New CAS Information Use Policies, enter HELP USAGETERMS for details.

This file supports REG1stRY for direct browsing and searching of all substance data from the REGISTRY file. Enter HELP FIRST for more information.

Searcher : Shears 571-272-2528

L8 4 L7

L8 ANSWER 1 OF 4 CAOLD COPYRIGHT 2006 ACS on STN
AN CA59:10228f CAOLD
TI synthesis of anticancerous substances - (I) derivs. of L-glutamic acid, (II) preparation of the N-p-[bis(β-chloroethyl)-amino]benzoyl-L-diethyl glutamate
AU Budeanu, Constantin H.; Druta, I. D.
IT 739-93-5 740-29-4 849-39-8 857-35-2 980-24-5 1584-35-6
1944-89-4 2311-25-3 2482-69-1 4271-30-1 **13726-52-8**
22536-03-4 60797-66-2 89364-91-0 89464-65-3 91252-97-0 91252-98-1
92109-21-2 92246-87-2 92249-19-9 93028-21-8 93028-22-9 93528-16-6
94313-36-7 94464-33-2 94754-67-3 96061-50-6 100916-11-8 111142-87-1

L8 ANSWER 2 OF 4 CAOLD COPYRIGHT 2006 ACS on STN
AN CA57:13866c CAOLD
TI steroids
PA CIBA Corp.
DT Patent
IT 1944-89-4 2467-87-0 3110-56-3 **13726-52-8** 17748-77-5
35152-81-9 91645-48-6 94754-67-3 96070-98-3 96378-03-9 96467-78-6
105403-74-5 105403-75-6 106067-70-3 106743-64-0 106743-65-1
106743-66-2 106822-45-1 106991-29-1 106991-30-4 107180-56-3

L8 ANSWER 3 OF 4 CAOLD COPYRIGHT 2006 ACS on STN
AN CA56:11695b CAOLD
TI synthesis of substances containing fragments of folic acid - (I) of glutamic acid derivs.
AU Alekseeva, L. V.; Pushkareva, Z. V.
IT 4271-30-1 **13726-52-8** 22536-03-4 93026-08-5 93060-83-4
93990-84-2 95767-54-7 98423-83-7 102379-14-6

L8 ANSWER 4 OF 4 CAOLD COPYRIGHT 2006 ACS on STN
AN CA52:361c CAOLD
TI metabolite analogs - (VII) preparation of benzimidazolyl analogs of ethyl pteroylglutamate
AU Siegart, William R.; Day, A. R.
IT 50-97-5 4271-30-1 **13726-52-8** 14625-39-9 17753-02-5
19018-24-7 19401-79-7 20033-95-8 20033-96-9 20033-97-0 20034-00-8
20034-02-0 22536-03-4 31490-20-7 59336-52-6 73259-50-4 95943-57-0
99846-87-4 99849-23-7 101257-52-7 101580-97-6 103853-48-1 104176-85-4
108244-38-8 109041-41-0 110514-28-8 110533-94-3 110534-25-3
111563-36-1 111825-01-5 114303-70-7 114381-53-2 114840-97-0
114840-99-2 118660-06-3 120581-90-0 122174-96-3

FILE 'USPATFULL' ENTERED AT 10:31:55 ON 21 MAR 2006
CA INDEXING COPYRIGHT (C) 2006 AMERICAN CHEMICAL SOCIETY (ACS)

FILE COVERS 1971 TO PATENT PUBLICATION DATE: 21 Mar 2006 (20060321/PD)
FILE LAST UPDATED: 21 Mar 2006 (20060321/ED)
HIGHEST GRANTED PATENT NUMBER: US7017190
HIGHEST APPLICATION PUBLICATION NUMBER: US2006059596
CA INDEXING IS CURRENT THROUGH 21 Mar 2006 (20060321/UPCA)
ISSUE CLASS FIELDS (/INCL) CURRENT THROUGH: 21 Mar 2006 (20060321/PD)
REVISED CLASS FIELDS (/NCL) LAST RELOADED: Feb 2006
USPTO MANUAL OF CLASSIFICATIONS THESAURUS ISSUE DATE: Feb 2006

L9 51 SEA ABB=ON PLU=ON L7

L10 24 SEA ABB=ON PLU=ON L9 AND (RA(S)ARTHRITIS OR RHEUMATOID? OR ANTIARTHRIT? OR ANTIRHEUMAT?)
L11 24 SEA ABB=ON PLU=ON L10 AND (TREAT? OR THERAP? OR PREVENT?)

L12 19 SEA ABB=ON PLU=ON L11 NOT (PY=>2004 OR PD=>20040116)

L12 ANSWER 1 OF 19 USPATFULL on STN
ACCESSION NUMBER: 2003:312713 USPATFULL
TITLE: New phenylalanine derivatives
INVENTOR(S): Suzuki, Nobuyasu, Kawasaki-shi, JAPAN
Yoshimura, Toshihiko, Kawasaki-shi, JAPAN
Izawa, Hiroyuki, Kawasaki-shi, JAPAN
Sagi, Kazuyuki, Kawasaki-shi, JAPAN
Makino, Shingo, Kawasaki-shi, JAPAN
Nakanishi, Eiji, Kawasaki-shi, JAPAN
Murata, Masahiro, Kawasaki-shi, JAPAN
Tsuji, Takashi, Kawasaki-shi, JAPAN
PATENT ASSIGNEE(S): AJINOMOTO CO. INC, Tokyo, JAPAN (non-U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2003220318	A1	20031127
APPLICATION INFO.:	US 2003-402006	A1	20030331 (10)

RELATED APPLN. INFO.: Continuation of Ser. No. WO 2001-JP8489, filed on 28 Sep 2001, UNKNOWN

	NUMBER	DATE
PRIORITY INFORMATION:	JP 2000-299490	20000929
	JP 2001-41885	20010219

DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: OBLON, SPIVAK, MCCLELLAND, MAIER & NEUSTADT, P.C., 1940 DUKE STREET, ALEXANDRIA, VA, 22314
NUMBER OF CLAIMS: 22
EXEMPLARY CLAIM: 1
LINE COUNT: 2128
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Specific phenylalanine derivatives or pharmaceutically acceptable. salts thereof have an antagonistic effect on the α4 integrins and, therefore, are usable as **therapeutic** agents or **preventive** agents for diseases in which α4 integrin-depending adhesion process participates in the pathology, such as inflammatory diseases, **rheumatoid** arthritis, inflammatory bowel diseases, systemic lupus erythematosus, multiple sclerosis, Sjogren's syndrome, asthma, psoriasis, allergy, diabetes, cardiovascular diseases, arterial sclerosis, restenosis, tumor proliferation, tumor metastasis and transplantation rejection.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L12 ANSWER 2 OF 19 USPATFULL on STN
ACCESSION NUMBER: 2003:251709 USPATFULL
TITLE: Inhibitors of alpha4mediated cell adhesion
INVENTOR(S): Kawaguchi, Takayuki, Tokyo, JAPAN
Nomura, Sumihiro, Saitama, JAPAN
Tsukimoto, Mikiko, Saitama, JAPAN
Kume, Toshiyuki, Saitama, JAPAN

	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 2003176498	A1	20030918	
APPLICATION INFO.:	US 2003-333985	A1	20030226	(10)
	WO 2001-US26594		20010827	

DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: BIRCH STEWART KOLASCH & BIRCH, PO BOX 747, FALLS CHURCH, VA, 22040-0747
NUMBER OF CLAIMS: 17
EXEMPLARY CLAIM: 1
LINE COUNT: 1599
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The present invention relates to a phenylalanine derivative of Formula (I) wherein X.sup.1 is a halogen atom, X.sup.2 is a halogen atom, Q is a CH.sub.2R-- is a carboxyl group which may be esterified; or a pharmaceutically acceptable salt thereof.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L12 ANSWER 3 OF 19 USPATFULL on STN
ACCESSION NUMBER: 2003:244962 USPATFULL
TITLE: Methotrexate derivatives
INVENTOR(S): Matsuoka, Hiroharu, Gotenba-shi, JAPAN
Suzuki, Hiroshi, Toshima-ku, JAPAN
Kato, Nobuaki, Gotenba-shi, JAPAN
Tsuji, Keiichiro, Gotenba-shi, JAPAN
Kuroki, Toshio, Gotenba-shi, JAPAN
Maruyama, Noriaki, Gotenba-shi, JAPAN
Nakagomi, Kazuya, Gotenba-shi, JAPAN
PATENT ASSIGNEE(S): CHUGAI SEIYAKU KABUSHIKI KAISHA, Tokyo, JAPAN (non-U.S. corporation)

	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 2003171376	A1	20030911	
APPLICATION INFO.:	US 2003-376711	A1	20030303	(10)

RELATED APPLN. INFO.: Division of Ser. No. US 1994-256441, filed on 12 Jul 1994, GRANTED, Pat. No. US 6559149 A 371 of International Ser. No. WO 1993-JP96, filed on 27 Jan 1993, UNKNOWN

	NUMBER	DATE
PRIORITY INFORMATION:	JP 1992-53051	19920127
	JP 1992-75106	19920213
	JP 1992-108320	19920316
	JP 1992-115126	19920324

DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: BROWDY AND NEIMARK, P.L.L.C., 624 NINTH STREET, NW, SUITE 300, WASHINGTON, DC, 20001-5303
NUMBER OF CLAIMS: 3
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 3 Drawing Page(s)
LINE COUNT: 1486
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB **Antirheumatic** agent containing as an active ingredient a

compound resented by the following general formula (II): ##STR1##

{where W is a group represented by the general formula: ##STR2##

[where R.sub.1 is a lower alkyl group having 1-4 carbon atoms; R.sub.2 is a lower alkyl group having 1-4 carbon atoms or a trifluoromethyl group; R.sub.3 is a hydrogen atom, a lower alkyl group having 1-4 carbon atoms or a trifluoromethyl group; R.sub.4 is a hydrogen atom or a lower alkyl group having 1-4 carbon atoms: R.sub.5 is a group represented by the general formula COOR.sub.6 (where R.sub.6 is a hydrogen atom or a lower alkyl group having 1-4 carbon atoms) or a group represented by the formula SO.sub.3H; and n is an integer of 1-4) or the general formula: ##STR3##

{where R7 is a lower alkyl group having 1-4 carbon atoms; R.sub.8 is a hydrogen atom or a lower alkyl group having 1-4 carbon atoms; R.sub.9 is a group represented by the general formula COOR.sub.10 (where R.sub.10 is a hydrogen atom or a lower alkyl group having 1-4 carbon atoms) or a group represented by the formula SO.sub.3H; and m is an integer of 1-4], or the general formula: ##STR4##

[where R.sub.11 is a hydrogen atom or a lower alkyl group having 1-4 carbon atoms; R.sub.12 is a hydrogen atom or a lower alkyl group having 1-4 carbon atoms; R.sub.13 is a group represent by the general formula COOR.sub.14 (where R.sub.14 is a hydrogen atom or a lower alkyl group having 1-4 carbon atoms) or a group represented by the formula SO.sub.3H; and l is an integer of 1 4], or the general formula: ##STR5##

[where R.sub.15 is a hydrogen atom or a lower alkyl group having 1-4 carbon atoms; R.sub.16 is a hydrogen atom or a lower alkyl group having 1-4 carbon atoms; and k is an integer of 2 or 3]}. All compounds represented by the general formula (II) 5 are novel except in the case where k is 2.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L12 ANSWER 4 OF 19 USPATFULL on STN

ACCESSION NUMBER:	2003:123345 USPATFULL
TITLE:	Methotrexate derivatives
INVENTOR(S):	Matsuoka, Hiroharu, Shizuoka, JAPAN Suzuki, Hiroshi, Tokyo, JAPAN Kato, Nobuaki, Shizuoka, JAPAN Tsuji, Keiichiro, Shizuoka, JAPAN Kuroki, Toshio, Shizuoka, JAPAN Maruyama, Noriaki, Shizuoka, JAPAN Nakagomi, Kazuya, Shizuoka, JAPAN
PATENT ASSIGNEE(S):	Chugai Seiyaku Kabushiki Kaisha, Tokyo, JAPAN (non-U.S. corporation)

	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 6559149	B1	20030506	
	WO 9315077		19930805	
APPLICATION INFO.:	US 1994-256441		19940712	(8)
	WO 1993-JP96		19930127	

	NUMBER	DATE

Searcher : Shears 571-272-2528

PRIORITY INFORMATION: JP 1992-53051 19920127
JP 1992-75106 19920213
JP 1992-108320 19920316.
JP 1992-115126 19920324
DOCUMENT TYPE: Utility
FILE SEGMENT: GRANTED
PRIMARY EXAMINER: Raymond, Richard L.
NUMBER OF CLAIMS: 8
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 3 Drawing Figure(s); 3 Drawing Page(s)
LINE COUNT: 1587
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB **Antirheumatic** agent containing as an active ingredient a compound resented by the following general formula (II): ##STR1##

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L12 ANSWER 5 OF 19 USPATFULL on STN
ACCESSION NUMBER: 2003:47794 USPATFULL
TITLE: Inhibitors of α4 mediated cell adhesion
INVENTOR(S): Sircar, Ila, San Diego, CA, United States
Gudmundsson, Kristjan S., Raleigh, NC, United States
Martin, Richard, San Diego, CA, United States
PATENT ASSIGNEE(S): Tanabe Seiyaku Co., Ltd., Osaka, JAPAN (non-U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 6521666	B1	20030218
APPLICATION INFO.:	US 2000-619712		20000719 (9)

RELATED APPLN. INFO.: Continuation of Ser. No. WO 1999-US993, filed on 19 Jan 1999

	NUMBER	DATE
PRIORITY INFORMATION:	US 1998-71840P	19980120 (60)

DOCUMENT TYPE: Utility
FILE SEGMENT: GRANTED
PRIMARY EXAMINER: Chang, Ceila
ASSISTANT EXAMINER: Small, Andrea D.
LEGAL REPRESENTATIVE: Birch, Stewart, Kolasch & Birch, LLP
NUMBER OF CLAIMS: 42
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 0 Drawing Figure(s); 0 Drawing Page(s)
LINE COUNT: 5451
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB ##STR1##

The present invention relates to a pharmaceutical composition comprising as an active ingredient a compound of formula (I), wherein Ring A is an aromatic or a heterocyclic ring; Q is a bond, carbonyl, lower alkylene, lower alkenylene, --O-(lower alkylene)-, etc.; n is 0, 1 or 2; Z is oxygen or sulfur, W is oxygen, sulfur, --CH.dbd.CH--, --NH-- or --N.dbd.CH--; R.sup.1, R.sup.2 and R.sup.3 are the same or different and are hydrogen, halogen, hydroxyl, a substituted or unsubstituted lower alkyl group, a substituted or unsubstituted lower alkoxy group, a substituted or unsubstituted amino group, etc.; R.sup.4 is tetrazolyl, carboxyl group, amide or

ester; R.sup.5 is hydrogen, nitro, amino, hydroxyl, lower alkanoyl, lower alkyl etc.; R.sup.6 is selected from (a) a substituted or unsubstituted phenyl group, (b) a substituted or unsubstituted pyridyl group, (c) a substituted or unsubstituted thienyl group, (d) a substituted or unsubstituted benzofuranyl group, etc.; or a pharmaceutically acceptable salt thereof.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L12 ANSWER 6 OF 19 USPATFULL on STN
ACCESSION NUMBER: 2002:346922 USPATFULL
TITLE: Inhibitors of phospholipase enzymes
INVENTOR(S): Seehra, Jasbir S., Lexington, MA, United States
McKew, John C., Arlington, MA, United States
Lovering, Frank, Acton, MA, United States
Bemis, Jean E., Arlington, MA, United States
Xiang, YiBin, Acton, MA, United States
Chen, Lihren, Cambridge, MA, United States
Knopf, John L., Acton, MA, United States
PATENT ASSIGNEE(S): Genetics Institute, LLC, Cambridge, MA, United States (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 6500853	B1	20021231
APPLICATION INFO.:	US 2000-686616		20001011 (9)
RELATED APPLN. INFO.:	Continuation-in-part of Ser. No. US 1999-256062, filed on 24 Feb 1999, now abandoned		

	NUMBER	DATE
PRIORITY INFORMATION:	US 1998-113674P	19980228 (60)

DOCUMENT TYPE: Utility
FILE SEGMENT: GRANTED
PRIMARY EXAMINER: Chang, Ceila
ASSISTANT EXAMINER: Wright, Sonya
LEGAL REPRESENTATIVE: Mazzarese, Joseph M.
NUMBER OF CLAIMS: 19
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 0 Drawing Figure(s); 0 Drawing Page(s)
LINE COUNT: 4414
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB This invention concerns compounds and pharmaceutical compositions useful for **treating** or **preventing** inflammatory conditions in a mammal, the methods comprising administration of novel pharmaceutically useful compounds of the general formulae: ##STR1##

or pharmaceutically acceptable salts thereof, wherein R.sub.1-R.sub.5 are as defined in the specification.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L12 ANSWER 7 OF 19 USPATFULL on STN
ACCESSION NUMBER: 2002:57787 USPATFULL
TITLE: Combination of benzoquinazoline antifolates and protecting agents
INVENTOR(S): Smith, Gary Keith, Raleigh, NC, United States
Duch, David Stanley, Cary, NC, United States

	Ferone, Robert, Raleigh, NC, United States
	Koch, Arthur, Bloomington, IN, United States
PATENT ASSIGNEE(S):	SmithKline Beecham Corporation, Philadelphia, PA, United States (U.S. corporation)

	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 6358952	B1	20020319	
	WO 9414448		19940707	
APPLICATION INFO.:	US 1995-448393		19950606	(8)
	WO 1993-GB2611		19931221	
			19950606	PCT 371 date

	NUMBER	DATE
PRIORITY INFORMATION:	GB 1992-26842	19921223

DOCUMENT TYPE:	Utility
FILE SEGMENT:	GRANTED
PRIMARY EXAMINER:	Goldberg, Jerome D.
LEGAL REPRESENTATIVE:	Lemanowicz, John L.
NUMBER OF CLAIMS:	11
EXEMPLARY CLAIM:	1
NUMBER OF DRAWINGS:	0 Drawing Figure(s); 0 Drawing Page(s)
LINE COUNT:	987

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The use of a protecting agent, for example a folate derivative such as folic acid or leucovorin, in combination with a non-competitive folic acid analogue, for example benzoquinazoline derivatives, for use in reducing the side effects associated with the administration of such non-competitive folic acid analogues; and pharmeceutical formulations comprising such combinations are disclosed.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L12 ANSWER 8 OF 19 USPATFULL on STN

ACCESSION NUMBER:	2001:79155 USPATFULL
TITLE:	Phosphodiesterase 4-inhibiting diazepinoindolones
INVENTOR(S):	Pascal, Yves, Rueil Malmaison, France
	Burnouf, Catherine, Ste Grenevieve-des-Bois, France
	Gaudilliere, Bernard, Nanterre, France
	Jacobelli, Henry, Paray Vieille Poste, France
	Calvet, Alain, Ann Arbor, MI, United States
	Payne, Adrian, Westerham, United Kingdom
	Dahl, Svein, Tromsdalen, Norway
PATENT ASSIGNEE(S):	Warner-Lambert Company, Morris Plains, NJ, United States (U.S. corporation)

	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 6239130	B1	20010529	
	WO 9849169		19981105	
APPLICATION INFO.:	US 1999-380883		19991110	(9)
	WO 1998-EP2827		19980430	
			19991110	PCT 371 date
			19991110	PCT 102(e) date

	NUMBER	DATE
PRIORITY INFORMATION:	FR 1997-5422	19970430

DOCUMENT TYPE: Utility
FILE SEGMENT: Granted
PRIMARY EXAMINER: Kifle, Bruck
LEGAL REPRESENTATIVE: Ashbrook, Charles W.
NUMBER OF CLAIMS: 24
EXEMPLARY CLAIM: 1
LINE COUNT: 2890
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB ##STR1##

The present invention presents compounds that inhibit phosphodiesterase 4 having Formula (I). The present invention also provides methods of using the compounds of Formula (I) to **prevent** or **treat** asthma, atopic dermatitis, **rheumatoid** arthritis, inflammatory bowel disorders, pulmonary hypertension, liver injury, bone loss, septic shock, or multiple sclerosis, and to pharmaceutical compositions that contain the compounds of Formula (I).

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L12 ANSWER 9 OF 19 USPATFULL on STN
ACCESSION NUMBER: 1999:170627 USPATFULL
TITLE: Pyridyl substituted imidazoles
INVENTOR(S): Adams, Jerry Leroy, Wayne, PA, United States
Gallagher, Timothy Francis, Harleysville, PA, United States
Garigipati, Ravi Shanker, Wayne, PA, United States
PATENT ASSIGNEE(S): SmithKline Beecham Corporation, Philadelphia, PA, United States (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 6008235		19991228
APPLICATION INFO.:	US 1997-995086		19971219 (8)

RELATED APPLN. INFO.: Division of Ser. No. US 1994-256499, filed on 22 Nov 1994, now patented, Pat. No. US 5716972 which is a continuation of Ser. No. WO 1993-US675, filed on 13 Jan 1993 which is a continuation-in-part of Ser. No. US 1993-819552, filed on 13 Jan 1993, now abandoned
DOCUMENT TYPE: Utility
FILE SEGMENT: Granted
PRIMARY EXAMINER: Fan, Jane
LEGAL REPRESENTATIVE: Dinner, Dara L., Venetianer, Stephen, Kinzig, Chaarles M.
NUMBER OF CLAIMS: 17
EXEMPLARY CLAIM: 1
LINE COUNT: 1345
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The novel compounds of Formula (I) have been found to be useful cytokine suppressive agents and therefore useful in the **treatment** and prophylaxis of disease states mediated thereby.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L12 ANSWER 10 OF 19 USPATFULL on STN
ACCESSION NUMBER: 1998:108412 USPATFULL

TITLE: Inhibition of matrix metalloproteases by substituted phenalkyl compounds
INVENTOR(S): Wolanin, Donald J., Orange, CT, United States
PATENT ASSIGNEE(S): Bayer Corporation, Pittsburgh, PA, United States (U.S. corporation)

	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 5804581		19980908	
APPLICATION INFO.:	US 1997-856696		19970515	(8)

DOCUMENT TYPE: Utility
FILE SEGMENT: Granted
PRIMARY EXAMINER: Ramsuer, Robert W.
NUMBER OF CLAIMS: 7
EXEMPLARY CLAIM: 1
LINE COUNT: 1347
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Matrix metalloprotease inhibiting compounds, pharmaceutical compositions thereof and a method of disease **treatment** using such compounds are presented. The compounds of the invention have the generalized formula: ##STR1## wherein T is a substituent and R.sup.24 is a substituted amide moiety. These compounds are useful for inhibiting matrix metalloproteases and, therefore, combating conditions to which MMP's contribute, such as osteoarthritis, **rheumatoid** arthritis, septic arthritis, periodontal disease, corneal ulceration, proteinuria, aneurysmal aortic disease, dystrophobic epidermolysis, bullosa, conditions leading to inflammatory responses, osteopenias mediated by MMP activity, tempera mandibular joint disease, demyelating diseases of the nervous system, tumor metastasis or degenerative cartilage loss following traumatic joint injury, and coronary thrombosis from athrosclerotic plaque rupture. The present invention also provides pharmaceutical compositions and methods for **treating** such conditions.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L12 ANSWER 11 OF 19 USPATFULL on STN
ACCESSION NUMBER: 1998:92039 USPATFULL
TITLE: Tricyclic compounds with pharmaceutical activity
INVENTOR(S): Boyle, Francis Thomas, Congleton, Great Britain
Crook, James William, Cheadle, Great Britain
Matusiak, Zbigniew Stanley, Holmes Chapel, Great Britain
PATENT ASSIGNEE(S): Zeneca Limited, London, United Kingdom (non-U.S. corporation)
British Technology Group Ltd., London, United Kingdom (non-U.S. corporation)

	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 5789417		19980804	
	WO 9411354		19940526	
APPLICATION INFO.:	US 1995-432161		19950628	(8)
	WO 1993-GB2281		19931104	
			19950628	PCT 371 date
			19950628	PCT 102(e) date

NUMBER DATE

Searcher : Shears 571-272-2528

PRIORITY INFORMATION:	GB 1992-23352	19921106
DOCUMENT TYPE:	Utility	
FILE SEGMENT:	Granted	
PRIMARY EXAMINER:	Ford, John M.	
LEGAL REPRESENTATIVE:	Pillsbury Madison & Sutro, LLP Intellectual Property Group	
NUMBER OF CLAIMS:	11	
EXEMPLARY CLAIM:	1	
LINE COUNT:	2009	

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The invention relates to tricyclic compounds of formula (I) ##STR1## wherein R.sup.1 is hydrogen, amino, (1-4C)alkyl, (1-4C)alkoxy, hydroxy-(1-4C)alkyl or fluoro-(1-4C)alkyl; R.sup.2 is hydrogen, (1-4C)alkyl, (3-4C)alkenyl, (3-4C)alkynyl, hydroxy-(2-4C)alkyl, halogeno-(2-4C)alkyl or cyano-(1-4C)alkyl; Ar is optionally-substituted phenylene, thiophenediyl, thiazolediyl, pyridinediyl or pyrimidinediyl; and R.sup.3 includes a group of the formula --NHCH(CO.sub.2 H)--A.sup.1 --Y.sup.1 wherein A.sup.1 is (1-6C)alkylene and Y.sup.1 is carboxy, tetrazol-5-yl, N-[(1-4C)alkylsulphonyl]carbamoyl, N(phenylsulphonyl)carbamoyl, tetrazol-5-ylthio, tetrazol-5-ylsulphinyl or tetrazol-5-ylsulphonyl; or pharmaceutically-acceptable salts or esters thereof; to processes for their manufacture; to pharmaceutical compositions containing them; and to their use as anti-cancer agents.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L12 ANSWER 12 OF 19 USPATFULL on STN

ACCESSION NUMBER:	1998:48417 USPATFULL			
TITLE:	Anti-cancer compounds			
INVENTOR(S):	Bavetsias, Vassilios, Sutton, England Boyle, Francis Thomas, Cangleton, England Hennequin, Laurent Francois Andre, Reims Cedex, France Marriott, Jonathan Hugh, Sutton, England			
PATENT ASSIGNEE(S):	British Technology Group Limited, London, England (non-U.S. corporation)			
	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 5747499		19980505	
	WO 9530673		19951116	
APPLICATION INFO.:	US 1996-732273		19961029	(8)
	WO 1995-GB1016		19950504	
			19961029	PCT 371 date
			19961029	PCT 102(e) date

	NUMBER	DATE
PRIORITY INFORMATION:	GB 1994-8936	19940505
DOCUMENT TYPE:	Utility	
FILE SEGMENT:	Granted	
PRIMARY EXAMINER:	Grumbling, Matthew V.	
LEGAL REPRESENTATIVE:	Nixon & Vanderhye	
NUMBER OF CLAIMS:	13	
EXEMPLARY CLAIM:	1	
LINE COUNT:	3719	

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Cyclopentaquinazoline of the formula (I): ##STR1## wherein R.sup.1 is hydrogen, amino, C.sub.1-4 alkyl, C.sub.1-4 alkoxy, C.sub.1-4 hydroxyalkyl or C.sub.1-4 fluoroalkyl;

wherein R.sup.2 is hydrogen, C.sub.1-4 alkyl, C.sub.3-4 alkenyl, C.sub.3-4 alkynyl, C.sub.2-4 hydroxyalkyl, C.sub.2-4 halogenoalkyl or C.sub.1-4 cyanoalkyl;

Ar.sup.1 is phenylene, thiophenediyl, thiazolediyl, pyridinediyl or pyrimidinediyl which may optionally bear one or two substituents selected from halogeno, hydroxy, amino, nitro, cyano, trifluoromethyl, C.sub.1-4 alkyl and C.sub.1-4 alkoxy; and

wherein R.sup.3 is a group of the formula:

--A.sup.1 --Ar.sup.2 --A.sup.2 --Y.sup.1

in which A.sup.1, A.sub.2, Y.sup.1 and Ar.sub.2 are defined in claim 1;

or a pharmaceutically acceptable salt or ester there of are of **therapeutic** value particularly in the **treatment** of cancer.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L12 ANSWER 13 OF 19 USPATFULL on STN

ACCESSION NUMBER:	1998:14819 USPATFULL			
TITLE:	Pyridyl substituted imidazoles			
INVENTOR(S):	Adams, Jerry Leroy, Wayne, PA, United States Gallagher, Timothy Francis, Harleysville, PA, United States Garigipati, Ravi Shanker, Wayne, PA, United States			
PATENT ASSIGNEE(S):	SmithKline Beecham Corporation, Philadelphia, PA, United States (U.S. corporation)			
	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 5716972		19980210	
APPLICATION INFO.:	US 1994-256499		19941122	(8)
	WO 1993-US675		19930113	
			19941122	PCT 371 date
			19941122	PCT 102(e) date
DOCUMENT TYPE:	Utility			
FILE SEGMENT:	Granted			
PRIMARY EXAMINER:	Fan, Jane			
LEGAL REPRESENTATIVE:	Dinner, Dara L., Venetianer, Stephen, Lentz, Edward T.			
NUMBER OF CLAIMS:	18			
EXEMPLARY CLAIM:	1			
LINE COUNT:	1354			

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The novel compounds of Formula (I) have been found to be useful cytokine suppressive agents and therefore useful in the **treatment** and prophylaxis of disease states mediated thereby.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L12 ANSWER 14 OF 19 USPATFULL on STN
ACCESSION NUMBER: 96:63112 USPATFULL
TITLE: Antiinflammatory and antineoplastic 5-deazaaminopterins and 5,10-dideazaaminopterins
INVENTOR(S): DeGraw, Joseph I., Sunnyvale, CA, United States
Colwell, William T., Menlo Park, CA, United States
Sirotnak, Francis M., New York, NY, United States
Smith, R. Lane, Palo Alto, CA, United States
Piper, James R., Birmingham, AL, United States
PATENT ASSIGNEE(S): SRI International, Menlo Park, CA, United States (U.S. corporation)
Sloan-Kettering Institute, New York, NY, United States (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 5536724		19960716
APPLICATION INFO.:	US 1993-140793		19931021 (8)

RELATED APPLN. INFO.: Continuation-in-part of Ser. No. US 1993-90750, filed on 12 Jul 1993, now patented, Pat. No. US 5354751 which is a continuation-in-part of Ser. No. US 1993-28431, filed on 9 Mar 1993, now patented, Pat. No. US 5374726 And a continuation-in-part of Ser. No. US 1993-8919, filed on 26 Jan 1993, now abandoned And a continuation-in-part of Ser. No. US 1992-938105, filed on 31 Aug 1992, now abandoned And a continuation-in-part of Ser. No. US 1992-845407, filed on 3 Mar 1992, now abandoned And a continuation-in-part of Ser. No. US 1992-875779, filed on 29 Apr 1992, now abandoned
DOCUMENT TYPE: Utility
FILE SEGMENT: Granted
PRIMARY EXAMINER: Berch, Mark L.
LEGAL REPRESENTATIVE: Verny, Hana
NUMBER OF CLAIMS: 24
EXEMPLARY CLAIM: 1,6,9,10,11
LINE COUNT: 2419
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Antiinflammatory and antineoplastic 5-deazaaminopterins and 5,10-dideazaaminopterins and their 5 and 10 alkyl analogs. A method for the **treatment** and **prevention** of inflammatory disease, such as **rheumatoid** arthritis, and for suppression and **prevention** of neoplastic growth in tumors and in blood forming tissues. A process for preparation of 10-deazaaminopterins.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L12 ANSWER 15 OF 19 USPATFULL on STN
ACCESSION NUMBER: 95:75960 USPATFULL
TITLE: Binding of E-selectin or P-selectin to sialyl Lewis.sup.x or sialyl-Lewis.sup.a
INVENTOR(S): Kogan, Timothy P., Sugar Land, TX, United States
Dupre, Brian, Houston, TX, United States
Scott, Ian L., Houston, TX, United States
Keller, Karin, Houston, TX, United States
Dao, Huong, Houston, TX, United States
Beck, Pamela J., Houston, TX, United States
PATENT ASSIGNEE(S): Texas Biotechnology Corporation, Houston, TX, United States (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 5444050		19950822
APPLICATION INFO.:	US 1994-235293		19940429 (8)
DOCUMENT TYPE:	Utility		
FILE SEGMENT:	Granted		
PRIMARY EXAMINER:	Robinson, Douglas W.		
ASSISTANT EXAMINER:	Fonda, Kathleen Kahler		
LEGAL REPRESENTATIVE:	Dressler, Goldsmith, Shore & Milnamow, Ltd.		
NUMBER OF CLAIMS:	19		
EXEMPLARY CLAIM:	1		
LINE COUNT:	1637		

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB This invention relates to compounds that inhibit the binding of E-selectin and/or P-selectin to sialyl-Lewis.sup.x or sialyl-Lewis.sup.a presented on a cell surface having the general structure ##STR1## wherein X is selected from the group consisting of --(CH.sub.2).sub.n CO.sub.2 H, --O(CH.sub.2).sub.m CO.sub.2 H, --(CH.sub.2).sub.n O(CH.sub.2).sub.m CO.sub.2 H, --CONH(CH.sub.2).sub.m CO.sub.2 H, --CH(OZ)(CO.sub.2 H), --CH(Z)(CO.sub.2 H), --(CH.sub.2).sub.n SO.sub.3 H, --(CH.sub.2).sub.n PO.sub.3 D.sub.1 D.sub.2, --NH(CH.sub.2).sub.m CO.sub.2 H, --CONH(CHR.sub.6)CO.sub.2 H, (1-H-tetrazolyl-5-alkyl-), and --OH;

R.sub.1 and R.sub.2 are independently selected from the group consisting of hydrogen, alkyl, halogen, --OZ, --NO.sub.2, --NH.sub.2 and --NHZ;

R.sub.3 is selected from the group consisting of hydrogen, halogen, alkyl, --OZ and --NHZ;

R.sub.4 is selected from the group consisting of hydrogen, halogen, alkyl, hydroxyl, hydroxyl-O-sulfate and --OZ;

R.sub.5 is selected from the group consisting of hydroxyl, --CN, --N.sub.3, --NH.sub.2, --NHNH.sub.2, --NE.sub.1 E.sub.2, --NHE.sub.1, --NHCO(CH.sub.2).sub.n CO.sub.2 H, --S(CH.sub.2).sub.m CO.sub.2 H and --NHCHNHNH.sub.2 ;

R.sub.6 is selected from the group consisting of hydrogen, alkyl, aralkyl, hydroxyalkyl, aminoalkyl, alkyl carboxylic acid and alkyl carboxamide;

wherein n is 0 to 6, m is 1 to 6, p is 0 to 6, b is 0 to 2, Z is alkyl, aryl or aralkyl, D.sub.1 and D.sub.2 are independantly hydrogen or alkyl, E.sub.1 is alkyl or --(CH.sub.2).sub.8 CO.sub.2 H, and E.sub.2 is alkyl, and the pharmaceutically acceptable salts, esters, amides, and prodrugs thereof. This invention also relates to methods of inhibiting the binding of E-selectin and/or P-selectin to sialyl-Lewis.sup.x or sialyl-Lewis.sup.a presented on a cell surface using said compounds and to pharmaceutically active compositions comprising compounds that inhibit the binding of E-selectin to sialyl-Lewis.sup.x and to methods of **treatment** of septic shock, ARDS, Crohn's disease, chronic inflammatory diseases, such as psoriasis and **rheumatoid** arthritis, and reperfusion injuries that occur following heart attacks, strokes and organ transplants.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L12 ANSWER 16 OF 19 USPATFULL on STN

ACCESSION NUMBER:	94:88696 USPATFULL
TITLE:	Methotrexate derivative
INVENTOR(S):	Ohi, Nobuhiro, Shizuoka, Japan Matsuoka, Hiroharu, Shizuoka, Japan Miyamoto, Katushito, Shizuoka, Japan Suzuki, Hiroshi, Shizuoka, Japan Kato, Nobuaki, Shizuoka, Japan Tsuji, Keiichiro, Shizuoka, Japan Takeda, Yasuhisa, Kanagawa, Japan Mihara, Masahiko, Shizuoka, Japan Nishina, Hiromichi, Shizuoka, Japan Shimaoka, Shin, Shizuoka, Japan Akamatsu, Kenichi, Shizuoka, Japan
PATENT ASSIGNEE(S):	Chugai Seiyaku Kabushiki Kaisha, Tokyo, Japan (non-U.S. corporation)

	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 5354753		19941011	
	WO 9203436		19920305	
APPLICATION INFO.:	US 1993-971773		19930212	(7)
	WO 1991-JP1078		19910814	
			19930212	PCT 371 date
			19930212	PCT 102(e) date

	NUMBER	DATE
PRIORITY INFORMATION:	JP 1990-2214691	19900814
	JP 1990-2215639	19900815
	JP 1990-2253466	19900921
	JP 1990-2293107	19901030
	JP 1990-2331845	19901129
	JP 1991-3180626	19910419
	JP 1991-3185943	19910423
	JP 1991-3228158	19910530
	JP 1991-3247141	19910612
	JP 1991-3258301	19910703
	JP 1991-3279047	19910730

DOCUMENT TYPE:	Utility
FILE SEGMENT:	Granted
PRIMARY EXAMINER:	Shah, Mukund J.
ASSISTANT EXAMINER:	Gupta, Y. N.
LEGAL REPRESENTATIVE:	Browdy and Neimark
NUMBER OF CLAIMS:	7
EXEMPLARY CLAIM:	1
NUMBER OF DRAWINGS:	12 Drawing Figure(s); 12 Drawing Page(s)
LINE COUNT:	2156

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Disclosed is a compound represented by the formula: ##STR1## wherein R.sup.1 : CH.sub.2, CH.sub.2 CH.sub.2, CH.sub.2 O, CH.sub.2 S, CH.sub.2 SO; R.sup.2 : hydrogen atom, a lower alkyl group having 1 to 4 carbon atoms or a benzyl group; n: an integer of 1 to 4; R.sup.3 : COOR.sup.4, NHCOR.sup.5, CONR.sup.6 R.sup.7, PO.sub.3 H.sub.2, SO.sub.3 H.

The compound shows potent **antirheumatic** function, psoriasis curing function and carcinostatic function and has low toxicity whereby it is available as a medicine.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L12 ANSWER 17 OF 19 USPATFULL on STN
ACCESSION NUMBER: 94:88694 USPATFULL
TITLE: Heteroaroyl 10-deazaamino-pterine compounds and use for **rheumatoid** arthritis
INVENTOR(S): DeGraw, Joseph I., Sunnyvale, CA, United States
Colwell, William T., Menlo Park, CA, United States
Sirotnak, Francis M., New York, NY, United States
Smith, R. Lane, Palo Alto, CA, United States
Piper, James R., Birmingham, AL, United States
PATENT ASSIGNEE(S): SRI International, Menlo Park, CA, United States (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 5354751		19941011
APPLICATION INFO.:	US 1993-90750		19930712 (8)

RELATED APPLN. INFO.: Continuation-in-part of Ser. No. US 1993-28431, filed on 9 Mar 1993 And a continuation-in-part of Ser. No. US 1993-8919, filed on 26 Jan 1993 And a continuation-in-part of Ser. No. US 1992-938105, filed on 31 Aug 1992, now abandoned And a continuation-in-part of Ser. No. US 1992-845407, filed on 3 Mar 1992, now abandoned And a continuation-in-part of Ser. No. US 1992-875779, filed on 29 Apr 1992, now abandoned
DOCUMENT TYPE: Utility
FILE SEGMENT: Granted
PRIMARY EXAMINER: Daus, Donald G.
LEGAL REPRESENTATIVE: Dolezalova, Hana
NUMBER OF CLAIMS: 13
EXEMPLARY CLAIM: 1
LINE COUNT: 1778
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB There is disclosed certain heteroaroyl 10-deazaaminopterin and 5, 10 and 8, 10 di deazaminopterin compounds and their use for **treatment** of **rheumatoid** arthritis and related diseases and preparative process.

Also disclosed are 10 alkenyl-(and alkynyl) 10-deazaminopterins also disclosed for **treatment** of **rheumatoid** arthritis and for leukemia and ascites tumors and preparative process.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L12 ANSWER 18 OF 19 USPATFULL on STN
ACCESSION NUMBER: 94:24423 USPATFULL
TITLE: Trifluoromethylketone derivatives, processes for preparation thereof and use thereof
INVENTOR(S): Hemmi, Keiji, Tsukuba, Japan
Shima, Ichiro, Ibaraki, Japan
Imai, Keisuke, Tsukuba, Japan
Tanaka, Hirokazu, Tsuchiura, Japan
PATENT ASSIGNEE(S): Fujisawa Pharmaceutical Co., Ltd., Osaka, Japan

(non-U.S. corporation)

	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 5296591		19940322	
APPLICATION INFO.:	US 1991-805610		19911212	(7)

	NUMBER	DATE
PRIORITY INFORMATION:	GB 1990-28231	19901231
	GB 1991-19713	19910916

DOCUMENT TYPE: Utility
FILE SEGMENT: Granted
PRIMARY EXAMINER: Moezie, F. T.
LEGAL REPRESENTATIVE: Oblon, Spivak, McClelland, Maier & Neustadt
NUMBER OF CLAIMS: 6
EXEMPLARY CLAIM: 1
LINE COUNT: 1006
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The trifluoromethylketone derivatives (I) and pharmaceutically acceptable salts thereof have a human leukocyte elastase inhibiting activity and are useful as human leukocyte elastase inhibitors for **treating** or **preventing** degenerative diseases. The trifluoromethylketone derivatives (I) have the following formula: ##STR1## wherein R.sup.1 is C.sub.1-6 alkyl which has one or two substituents selected from carboxy, esterified carboxy and di-C.sub.1-6 alkylcarbamoyl; phenyl(C.sub.1-6) alkyl, the phenyl moiety of which may have halogen or nitro or amino substituents and the alkyl moiety of which may have carboxy or esterified carboxy substituents; halo-phenyl; morpholino; or morpholino(C.sub.1-6) alkyl,

R.sup.2 and R.sup.3 are each C.sub.1-6 alkyl,

X is -- or --NH--, and

Y is ##STR2## and pharmaceutically acceptable salts thereof.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L12 ANSWER 19 OF 19 USPATFULL on STN
ACCESSION NUMBER: 79:40694 USPATFULL
TITLE: Penicillamine compounds
INVENTOR(S): Shiroki, Masami, Nakatsu, Japan
Maruyama, Yutaka, Yoshitomimachi, Japan
Goto, Kazuhiro, Nakatsu, Japan
PATENT ASSIGNEE(S): Yoshitomi Pharmaceutical Industries, Ltd., Osaka, Japan (non-U.S. corporation)

	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 4169899		19791002	
APPLICATION INFO.:	US 1978-867413		19780106	(5)

	NUMBER	DATE
PRIORITY INFORMATION:	JP 1977-1008	19770108

DOCUMENT TYPE: Utility
FILE SEGMENT: Granted

Searcher : Shears 571-272-2528

PRIMARY EXAMINER: Ford, John M.
ASSISTANT EXAMINER: Fan, Jane T.
LEGAL REPRESENTATIVE: Sughrue, Rothwell, Mion, Zinn and Macpeak
NUMBER OF CLAIMS: 17
EXEMPLARY CLAIM: 1
LINE COUNT: 777
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Penicillamine compounds of the formula: ##STR1## and of the formula: ##STR2## wherein R.sup.1, R.sup.2, R.sup.3, A and B are as defined hereinafter, and pharmaceutically acceptable acid addition salts thereof are disclosed. II are the products of hydrolysis or alcoholysis of I, and I are in turn the products of dehydration of II or alcohol removal form II. I and II are useful for the **treatment** of **rheumatoid** arthritis.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

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L13 0 L7

(FILE 'REGISTRY' ENTERED AT 10:34:00 ON 21 MAR 2006)
E PEPTIDYLARGININE DEIMINASE/CN 5
L17 20 S PEPTIDYLARGININE DEIMINASE ?/CN

-Key terms

(FILE 'CAPLUS' ENTERED AT 10:48:51 ON 21 MAR 2006)
L17 20 SEA FILE=REGISTRY ABB=ON PLU=ON PEPTIDYLARGININE DEIMINASE ?/CN
L19 266 SEA FILE=CAPLUS ABB=ON PLU=ON L17 OR (PEPTID!LARGININE OR (PROTEIN OR PEPTID!L)(W)(ARGININE OR ARG))(W)DEIMINASE OR PAD(S)(PEPTID?(1W)DEIMINASE)
L20 72 SEA FILE=CAPLUS ABB=ON PLU=ON L19 AND (RA(S)ARTHRITIS OR RHEUMATOID? OR ANTIARTHRIT? OR ANTIRHEUMAT?)
L21 20 SEA FILE=CAPLUS ABB=ON PLU=ON L20 AND (TREAT? OR THERAP? OR PREVENT? OR PROPHYLAX? OR PROPHYLACT?)
L22 3 SEA FILE=CAPLUS ABB=ON PLU=ON L21 NOT (PY=>2004 OR PD=>20040116)

L23 3 S L22 NOT L6

L23 ANSWER 1 OF 3 CAPLUS COPYRIGHT 2006 ACS on STN
ED Entered STN: 29 Jun 2001
ACCESSION NUMBER: 2001:472747 CAPLUS
DOCUMENT NUMBER: 135:91514
TITLE: Peptides designed for the diagnosis and **treatment** of **rheumatoid** arthritis
INVENTOR(S): Union, Ann; Moereels, Henri; Meheus, Lydie
PATENT ASSIGNEE(S): Innogenetics N.V., Belg.
SOURCE: PCT Int. Appl., 53 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent

LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001046222	A2	20010628	WO 2000-EP13037	20001220
WO 2001046222	A3	20020117		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2391356	AA	20010628	CA 2000-2391356	20001220
EP 1240180	A2	20020918	EP 2000-983355	20001220
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
US 2002143143	A1	20021003	US 2000-747029	20001221
PRIORITY APPLN. INFO.:			EP 1999-870280 A	19991221
			EP 2000-870195 A	20000908
			WO 2000-EP13037 W	20001220

AB The present invention relates to peptides that mimic the immunogenic determinants of self-proteins recognized by autoimmune antibodies in a biol. sample from patients suffering from **rheumatoid arthritis** (**RA**). More particularly, the present invention relates to citrulline-containing peptides, which react with the majority of the latter antibodies. Furthermore, the present invention relates to diagnostic tools for a more convenient and sensitive diagnosis of RA and to **therapeutical** methods to **treat** RA.

L23 ANSWER 2 OF 3 CAPLUS COPYRIGHT 2006 ACS on STN
ED Entered STN: 21 Jun 1999
ACCESSION NUMBER: 1999:380965 CAPLUS
DOCUMENT NUMBER: 131:31040
TITLE: Synthetic peptides containing citrulline recognized by **rheumatoid** arthritis sera as tools for diagnosis and **treatment**
INVENTOR(S): Meheus, Lydie; Union, Ann; Raymackers, Joseph
PATENT ASSIGNEE(S): Innogenetics N.V., Belg.
SOURCE: PCT Int. Appl., 74 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9928344	A2	19990610	WO 1998-EP7714	19981130
WO 9928344	A3	19990812		

W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

EP 949270	A1	19991013	EP 1998-870078	19980409
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
CA 2309534	AA	19990610	CA 1998-2309534	19981130
AU 9921558	A1	19990616	AU 1999-21558	19981130
EP 1034186	A2	20000913	EP 1998-965715	19981130
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
JP 2002512939	T2	20020508	JP 2000-523235	19981130
PRIORITY APPLN. INFO.:			EP 1997-870195 A	19971128
			EP 1998-870078 A	19980409
			WO 1998-EP7714 W	19981130

AB The present invention relates to a method of producing certain peptides containing citrulline residues that constitute immunogenic determinants of antibodies present in sera from patients with **rheumatoid** arthritis and wherein the presence of at least one citrulline is a prerequisite for reacting with said antibodies. The invention also relates to a method of producing said antibodies and the use of said peptides for diagnosis and **treatment** of **rheumatoid** arthritis. The citrulline-containing peptides, may be circularized or branched peptides and/or containing tandem repeats, are derived from variant of filaggrin, intermediate filament protein, vimentin, cytokeratin 1 or cytokeratin 9.

L23 ANSWER 3 OF 3 CAPLUS COPYRIGHT 2006 ACS on STN
ED Entered STN: 19 Jan 1999
ACCESSION NUMBER: 1999:33223 CAPLUS
DOCUMENT NUMBER: 130:195491
TITLE: The epitopes targeted by the **rheumatoid** arthritis-associated antifilaggrin autoantibodies are posttranslationally generated on various sites of (pro)filaggrin by deimination of arginine residues
AUTHOR(S): Girbal-Neuhauser, Elisabeth; Durieux, Jean-Jacques; Arnaud, Michel; Dalbon, Pascal; Sebbag, Mireille; Vincent, Christian; Simon, Michel; Senshu, Tatsuo; Masson-Bessiere, Christine; Jolivet-Reynaud, Colette; Jolivet, Michel; Serre, Guy
CORPORATE SOURCE: Department of Biology and Pathology of the Cell, Institut National de la Sante et de la Recherche MedicaleT, Toulouse-Purpan School of Medicine, University Toulouse III, Toulouse, Fr.
SOURCE: Journal of Immunology (1999), 162(1), 585-594
CODEN: JOIMA3; ISSN: 0022-1767
PUBLISHER: American Association of Immunologists
DOCUMENT TYPE: Journal

LANGUAGE: English

AB Antifilaggrin autoantibodies (AFA) are a population of IgG autoantibodies associated to **rheumatoid arthritis** (**RA**), which includes the so-called "antikeratin" Abs and antiperinuclear factor. AFA are the most specific serol. markers of RA. We previously showed that they recognize human epidermal filaggrin and other profilaggrin-related proteins of various epithelial tissues. Here, we report further characterization of the protein Ags and epitopes targeted by AFA. All the Ags that exhibit numerous neutral/acidic isoelec. variants were immunochem. demonstrated to be deiminated proteins. In vitro deimination of a recombinant human filaggrin by a **peptidylarginine deiminase** generated AFA epitopes on the protein. Moreover, two of three filaggrin-derived synthetic peptides with a citrulline in the central position were specifically and widely recognized by AFA affinity-purified from a series of RA sera. These results indicate that citrulline residues are constitutive of the AFA epitopes, but only in the context of specific amino acid sequences of filaggrin. In competition expts., the two peptides abolished the AFA reactivity of RA sera, showing that they present major AFA epitopes. These data should help in the identification of a putative deiminated AFA-inducing or cross-reactive articular autoantigen and provide new insights into the pathogenesis of RA. They could also open the way toward specific immunosuppressive and/or **preventive therapy** of RA.

REFERENCE COUNT: 56 THERE ARE 56 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

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L24 48 S L21
L25 28 DUP REM L24 (20 DUPLICATES REMOVED)

L25 ANSWER 1 OF 28 EMBASE COPYRIGHT (c) 2006 Elsevier B.V. All rights reserved on STN
ACCESSION NUMBER: 2006070692 EMBASE
TITLE: Genetic progress towards the molecular basis of

autoimmunity.
AUTHOR: Pearce S.H.S.; Merriman T.R.
CORPORATE SOURCE: S.H.S. Pearce, Institute of Human Genetics, International Centre for Life, University of Newcastle, Central Parkway, Newcastle upon Tyne, NE1 3BZ, United Kingdom. s.h.s.pearce@ncl.ac.uk
SOURCE: Trends in Molecular Medicine, (2006) Vol. 12, No. 2, pp. 90-98. .
Refs: 78
ISSN: 1471-4914 CODEN: TMMRCY
PUBLISHER IDENT.: S 1471-4914(05)00285-6
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 005 General Pathology and Pathological Anatomy
022 Human Genetics
026 Immunology, Serology and Transplantation
029 Clinical Biochemistry
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 20060303
Last Updated on STN: 20060303

AB The past few years have seen the identification of PTPN22 and the confirmation of CTLA-4 as common autoimmune disease genes. Together with MHC and INS, these developments have increased the collection of confirmed susceptibility loci for autoimmunity. In this article, the latest developments related to these genes and to other recently studied candidate autoimmune susceptibility loci (PDCD1, FCRL3, SUMO4, CD25, PADI4 and SLC22A4) are reviewed. Collectively, these genes strongly indicate that aberrant inhibition of the signalling cascade initiated by activation of the T-cell receptor is involved in the aetiology of autoimmune disease. However, much basic genetic, molecular and clinical research is still needed to help us fully understand the underlying mechanisms of autoimmunity and how these translate into prognosis or **therapy**. .COPYRGT. 2005 Elsevier Ltd. All rights reserved.

L25 ANSWER 2 OF 28 EMBASE COPYRIGHT (c) 2006 Elsevier B.V. All rights reserved on STN
ACCESSION NUMBER: 2006011473 EMBASE
TITLE: Use and significance of anti-CCP autoantibodies in **rheumatoid** arthritis.
AUTHOR: Zendman A.J.W.; van Venrooij W.J.; Pruijn G.J.M.
CORPORATE SOURCE: A.J.W. Zendman, Department of Biochemistry, Radboud University Nijmegen, PO Box 9101, 6500 HB Nijmegen, Netherlands. h.zendman@ncmls.ru.nl
SOURCE: Rheumatology, (2006) Vol. 45, No. 1, pp. 20-25. .
Refs: 75
ISSN: 1462-0324 CODEN: RUMAFK
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 005 General Pathology and Pathological Anatomy
026 Immunology, Serology and Transplantation
031 Arthritis and Rheumatism
037 Drug Literature Index
LANGUAGE: English
ENTRY DATE: Entered STN: 20060119
Last Updated on STN: 20060119
DATA NOT AVAILABLE FOR THIS ACCESSION NUMBER

L25 ANSWER 3 OF 28 MEDLINE on STN
ACCESSION NUMBER: 2006150980 IN-PROCESS
DOCUMENT NUMBER: PubMed ID: 16539813
TITLE: Antibodies against transglutaminases, **peptidylarginine deiminase** and citrulline in **rheumatoid** arthritis - new pathways to epitope spreading.
AUTHOR: Roth E B; Stenberg P; Book C; Sjoberg K
CORPORATE SOURCE: Hospital Pharmacy, Malmo University Hospital, Malmo, Sweden.
SOURCE: Clinical and experimental rheumatology, (2006 Jan-Feb) Vol. 24, No. 1, pp. 12-8.
Journal code: 8308521. ISSN: 0392-856X.
PUB. COUNTRY: Italy
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: NONMEDLINE; IN-DATA-REVIEW; IN-PROCESS; NONINDEXED; Priority Journals
ENTRY DATE: Entered STN: 20060317
Last Updated on STN: 20060317

AB OBJECTIVE:The findings of the involvement of tissue transglutaminase (tTg) in the pathogenesis of coeliac disease (CD) have stimulated progress in the field of auto-immune diseases. Another calcium-dependent cysteine enzyme, **peptidylarginine deiminase** type 4 (PAD4), seems to be involved in the pathogenesis of **rheumatoid arthritis** (**RA**). There are obvious similarities between Tgs and PADs. METHODS:Using enzyme-linked immuno-sorbent assays, we have measured the occurrence of antibodies against guinea pig (gp) and human recombinant (hr) tTg, PAD and citrulline in 59 controls and 184 RA-patients, of whom 71 were **treated** with methotrexate (mtx). RESULTS:In addition to the expected antibodies against citrulline (62%), sera from the 113 RA-patients without mtx **treatment** contained significantly increased frequencies of IgG anti-PAD (35%), IgA anti-gp-tTg (34%), IgA anti-hr tTg (20%), IgG anti-gp-tTg (13%) and IgA anti-hr-FXIII (15%) compared to controls. In sera from the mtx-**treated** RA-patients the expression of antibodies was reduced. In patients not **treated** with methotrexate there was a statistically significant correlation between, on one hand, IgG anti-PAD and on the other hand, IgG anti-citrulline, IgA anti-gp-tTg, IgA anti-hr-tTg, IgG anti-gp-tTg, IgG anti-hr-tTg, or IgA anti-hr-FXIII. In the mtx-**treated** group these correlations were less pronounced. CONCLUSION:In addition to the expected antibodies against citrulline, sera from RA-patients contained antibodies against PAD and against Tgs of at least two kinds, indicating that the specificity for anti-tTg in CD is far from complete. Most of the patients displayed more than one antibody, a possible indication of epitope spreading. MTX-**treatment** reduced the expression of antibodies.

L25 ANSWER 4 OF 28 WPIDS COPYRIGHT 2006 THE THOMSON CORP on STN
ACCESSION NUMBER: 2005-648942 [66] WPIDS
DOC. NO. CPI: C2005-195334
TITLE: Novel **peptidylarginine deiminase** type IV inhibitor arginine derivative compound or its salt, useful for **preventing** and/or **treating** diseases in which peptidyl arginine deaminase is involved e.g. **rheumatoid** arthritis and psoriasis.

Searcher : Shears 571-272-2528

DERWENT CLASS: B05
INVENTOR(S): HASHIMOTO, H; HIDAKA, Y; SATO, M; SHIMIZU, T; YAMADA, M
PATENT ASSIGNEE(S): (UYYO-N) UNIV YOKOHAMA CITY
COUNTRY COUNT: 108
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2005075414	A1	20050818	(200566)*	JA	52

RW: AT BE BG BW CH CY CZ DE DK EA EE ES FI FR GB GH GM GR HU IE IS IT KE LS LT LU MC MW MZ NA NL OA PL PT RO SD SE SI SK SL SZ TR TZ UG ZM ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BW BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE EG ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NA NI NO NZ OM PG PH PL PT RO RU SC SD SE SG SK SL SY TJ TM TN TR TT TZ UA UG US UZ VC VN YU ZA ZM ZW

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2005075414	A1	WO 2005-JP1574	20050203

PRIORITY APPLN. INFO: JP 2004-28467 20040204
AN 2005-648942 [66] WPIDS
AB WO2005075414 A UPAB: 20051014
NOVELTY - **Peptidylarginine deiminase** type IV inhibitor compound (C1), which is an arginine derivative, is new.
DETAILED DESCRIPTION - **Peptidylarginine deiminase** type IV inhibitor arginine derivative compound or its salt (C1) of formula (I).
R1-R3 = hydrogen or 1-3C alkyl group, where at least one of R1, R2 and R3 is not hydrogen;
R4 = substituted amino group;and
R5 = optionally substituted carboxyl group.
An INDEPENDENT CLAIM is also included for **peptidylarginine deiminase** type IV inhibitor (II), comprising (C1) as an active ingredient, where (C1) is capable of inhibiting a process in the reaction mechanism of **peptidylarginine deiminase** type IV having SEQ ID Number 1, and its reaction substrate.
ACTIVITY - **Antiarthritic; Antirheumatic;** Antipsoriatic; Neuroprotective.
MECHANISM OF ACTION - **Peptidylarginine deiminase** type IV inhibitor (claimed).
Ability of arginine derivative in inhibiting **peptidylarginine deiminase** type IV was studied as follows. Tris buffer, Bz-Arg and **peptidylarginine deiminase** type IV were mixed by ice cooling. Then, Bz-Arg(mono-methyl), NG-monomethyl-L-arginine, and NG,NG-dimethyl-L-arginine were mixed with the Bz-Arg solution and reacted at 37 deg. C for 60 minutes. The reaction was stop and the reaction mixture was separated by reverse phase high performance liquid chromatography (HPLC), and the inhibitory effect was studied. The results showed that the Bz-NG,NG-dimethyl-L-arginine derivative exhibited potent inhibitory activity.

USE - (II) is useful for **preventing** and/or **treating** diseases in which a peptidyl arginine deaminase is involved e.g. **rheumatoid** arthritis, psoriasis and multiple sclerosis (claimed).

ADVANTAGE - (C1) is a potent **peptidylarginine deiminase** type IV inhibitor.

DESCRIPTION OF DRAWING(S) - The figure shows a graph the results of inhibition reaction of **peptidylarginine deiminase** type IV by Bz-Arg derivative (reaction time = 60 minutes).

Dwg.4/4

L25 ANSWER 5 OF 28 WPIDS COPYRIGHT 2006 THE THOMSON CORP on STN

ACCESSION NUMBER: 2005-532167 [54] WPIDS
DOC. NO. CPI: C2005-161320
TITLE: **Treatment** of **rheumatoid** arthritis involves use of a composition comprising **peptidylarginine deiminase** inhibitor.
DERWENT CLASS: B05
INVENTOR(S): GLUCK, O S; MARICIC, M J
PATENT ASSIGNEE(S): (GLUC-I) GLUCK O S; (MARI-I) MARICIC M J
COUNTRY COUNT: 1
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
US 2005159334	A1	20050721	(200554)*		5

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
US 2005159334	A1	US 2004-759881	20040116

PRIORITY APPLN. INFO: US 2004-759881 20040116
AN 2005-532167 [54] WPIDS
AB US2005159334 A UPAB: 20050823
NOVELTY - **Treatment** of a host for **rheumatoid** arthritis involves administration of a composition comprising **peptidylarginine deiminase** (**PAD**) inhibitor.

ACTIVITY - **Antiarthritic; Antirheumatic.**

MECHANISM OF ACTION - **Peptidylarginine deiminase** (**PAD**) inhibitor.

USE - For the **treatment** of a host for **rheumatoid** arthritis (claimed).

ADVANTAGE - The method provides inhibition of the isoenzymes of PAD, to block the citrullination of proteins pivotal to the initiation and progression of **rheumatoid arthritis** (**RA**).

Dwg.0/1

L25 ANSWER 6 OF 28 MEDLINE on STN DUPLICATE 1

ACCESSION NUMBER: 2005385267 MEDLINE
DOCUMENT NUMBER: PubMed ID: 16023115
TITLE: Methylation of the guanidino group of arginine residues **prevents** citrullination by **peptidylarginine deiminase** IV.

Searcher : Shears 571-272-2528

AUTHOR: Hidaka Yuji; Hagiwara Teruki; Yamada Michiyuki
CORPORATE SOURCE: Department of Life Science, School of Science and Engineering, Kinki University, 3-4-1 Kowakae, Higashi-Osaka, Osaka 577-8502, Japan.. yuji@life.kindai.ac.jp
SOURCE: FEBS letters, (2005 Aug 1) Vol. 579, No. 19, pp. 4088-92.
Journal code: 0155157. ISSN: 0014-5793.
PUB. COUNTRY: Netherlands
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200509
ENTRY DATE: Entered STN: 20050727
Last Updated on STN: 20050917
Entered Medline: 20050916

AB **Peptidylarginine deiminase** IV (**PAD** IV) catalyzes the citrullination of Arg residues of proteins, such as histones. Suzuki et al. recently reported that haplotypes of the PAD IV gene are associated with susceptibility to **rheumatoid** arthritis. To investigate the mechanism of substrate specificity and inhibitors of PAD IV, a series of the Arg derivatives were synthesized and their reactivity to PAD IV examined. The results suggest that both imino and carboxyl groups are important in the molecular recognition of PAD IV and that methylation of the guanidino group **prevents** citrullination. In addition, the findings herein show that Bz-N(G)-monomethyl-Arg and Bz-N(G),N(G)-dimethyl-Arg specifically inhibit citrullination.

L25 ANSWER 7 OF 28 MEDLINE on STN DUPLICATE 2
ACCESSION NUMBER: 2005228243 MEDLINE
DOCUMENT NUMBER: PubMed ID: 15832289
TITLE: Humoral immune response to citrullinated collagen type II determinants in early **rheumatoid** arthritis.
AUTHOR: Burkhardt Harald; Sehnert Bettina; Bockermann Robert; Engstrom Ake; Kalden Jochen R; Holmdahl Rikard
CORPORATE SOURCE: Department of Internal Medicine III and Institute of Clinical Immunology, University of Erlangen-Nuremberg, Erlangen, Germany.. Harald.Burkhardt@med3.imed.uni-erlangen.de
SOURCE: European journal of immunology, (2005 May) Vol. 35, No. 5, pp. 1643-52.
Journal code: 1273201. ISSN: 0014-2980.
PUB. COUNTRY: Germany: Germany, Federal Republic of
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200506
ENTRY DATE: Entered STN: 20050503
Last Updated on STN: 20050629
Entered Medline: 20050628

AB Collagen type II (CII) is a relevant joint-specific autoantigen in the pathogenesis of **rheumatoid arthritis** (**RA**). Whereas the reasons for the breakage of self tolerance to this major cartilage component are still enigmatic, T cell responses to glycosylated CII determinants in RA patients indicate that post-translational modifications play a role. Since the conversion of arginine into citrulline by **peptidylarginine**

deiminases (**PAD**) in some non-joint-specific antigens such as filaggrin or fibrin has been shown to give rise to RA-specific humoral immune responses, we investigated whether **PAD** modification of cartilage-specific CII might affect its recognition by circulating autoantibodies in early RA. In vitro **treatment** with purified PAD led to arginine deimination of native CII or of synthetic CII peptides as evidenced by amino acid analysis. The citrullination resulted in modified recognition of the immunodominant CII epitope C1(III) (amino acid residues 359-369) by murine and human antibodies. In a cohort of early RA patients (n=286), IgG antibodies directed toward a synthetic citrullinated C1(III) peptide (citC1(III)-P) were detectable with a prevalence of 40.4%. The partial autoantibody cross-reactivity between citC1(III)-P and citrullinated peptides mimicking epitopes of the cytoskeletal autoantigen filaggrin suggests that autoimmunity to cartilage-specific modified self might be a critical intermediate bridging recognition of PAD-modified extra-articular autoantigens with the disruption of tolerance to native cartilage constituents.

L25 ANSWER 8 OF 28 MEDLINE on STN DUPLICATE 3
ACCESSION NUMBER: 2005598436 MEDLINE
DOCUMENT NUMBER: PubMed ID: 16277695
TITLE: Identification of citrullinated alpha-enolase as a candidate autoantigen in **rheumatoid** arthritis.
AUTHOR: Kinloch Andrew; Tatzer Verena; Wait Robin; Peston David; Lundberg Karin; Donatien Phillipe; Moyes David; Taylor Peter C; Venables Patrick J
CORPORATE SOURCE: Kennedy Institute of Rheumatology, Imperial College London, Charing Cross Hospital Campus, 1 Aspenlea Road, London W6 8LH, UK.
SOURCE: Arthritis research & therapy, (2005) Vol. 7, No. 6, pp. R1421-9. Electronic Publication: 2005-10-19. Journal code: 101154438. E-ISSN: 1478-6362.
PUB. COUNTRY: England: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200601
ENTRY DATE: Entered STN: 20051110
Last Updated on STN: 20060111
Entered Medline: 20060110

AB Antibodies against citrullinated proteins are highly specific for **rheumatoid arthritis** (**RA**), but little is understood about their citrullinated target antigens. We have detected a candidate citrullinated protein by immunoblotting lysates of monocytic and granulocytic HL-60 cells **treated** with **peptidylarginine deiminase**. In an initial screen of serum samples from four patients with RA and one control, a protein of molecular mass 47 kDa from monocytic HL-60s reacted with sera from the patients, but not with the serum from the control. Only the citrullinated form of the protein was recognised. The antigen was identified by tandem mass spectrometry as alpha-enolase, and the positions of nine citrulline residues in the sequence were determined. Serum samples from 52 patients with RA and 40 healthy controls were tested for presence of antibodies against citrullinated and non-citrullinated alpha-enolase by immunoblotting of the purified antigens. Twenty-four sera from patients with RA (46%) reacted with citrullinated alpha-enolase, of which seven (13%) also recognised the

non-citrullinated protein. Six samples from the controls (15%) reacted with both forms. Alpha-enolase was detected in the RA joint, where it co-localised with citrullinated proteins. The presence of antibody together with expression of antigen within the joint implicates citrullinated alpha-enolase as a candidate autoantigen that could drive the chronic inflammatory response in RA.

L25 ANSWER 9 OF 28 JICST-EPlus COPYRIGHT 2006 JST on STN
ACCESSION NUMBER: 1050443593 JICST-EPlus
TITLE: Forefront of medicine and medical **treatment**. **Rheumatoid** arthritis and citrulline antigen.
AUTHOR: YAMAMOTO KAZUHIKO
YAMADA RYO
CORPORATE SOURCE: Fac. Medicine, Univ. Tokyo, JPN
Inst. of Physical and Chemical Res.
SOURCE: Nippon Naika Gakkai Zasshi (Journal of the Japanese Society of Internal Medicine), (2005) vol. 94, no. 5, pp. 984-989. Journal Code: F0916A (Fig. 2, Ref. 10)
CODEN: NNGAAS; ISSN: 0021-5384
PUB. COUNTRY: Japan
DOCUMENT TYPE: Journal; Commentary
LANGUAGE: Japanese
STATUS: New
AB It was clarified that PADI4 is related to RA in 5 genes which encoded the enzyme of **peptidyl arginine deiminase** (PADI). It was confirmed that Japanese largely had two PADI4 gene haplotypes, which were divided into a gene with RA sensitivity and a gene with RA nonsensibility and that the stability was high on the transcriptional product from the gene with RA sensitivity. The PADI has the movement which replaces the arginine residue in the protein with the citrulline. It is considered that the citrulline by PADI4 is accelerated in RA, and as the result, the change is generated in quality and quantity of citrulline of the self peptide, which causes the failure of the immunologic tolerance. And, the specificity of anti-CCP antibody used widely as a system which measures anti-citrulline autoantibody is as high as 80 to 98%, and it is proven that the bone and cartilage destruction progresses further in patients with anti-CCP antibody positive. It seems to be an important autoantibody for diagnosis of RA.

L25 ANSWER 10 OF 28 EMBASE COPYRIGHT (c) 2006 Elsevier B.V. All rights reserved on STN
ACCESSION NUMBER: 2005580832 EMBASE
TITLE: Genetic basis of **rheumatoid** arthritis.
AUTHOR: Dieude P.; Cornelis F.
CORPORATE SOURCE: F. Cornelis, GenHotel - EA3886, European Research Laboratory for Rheumatoid Arthritis, Evry-Paris 7 University, 2, rue Gaston Cremieux, 91000 Evry, France. francois.cornelis@lrb.ap-hop-paris.fr
SOURCE: Joint Bone Spine, (2005) Vol. 72, No. 6, pp. 520-526. .
Refs: 63
ISSN: 1297-319X CODEN: JBSPFA
PUBLISHER IDENT.: S 1297-319X(05)00159-4
COUNTRY: France
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 005 General Pathology and Pathological Anatomy
022 Human Genetics
031 Arthritis and Rheumatism
LANGUAGE: English

Searcher : Shears 571-272-2528

SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 20060202
Last Updated on STN: 20060202

AB **Rheumatoid arthritis** (**RA**) is a multifactorial disease due to a combination of genetic and environmental factors. Identification of the genetic factors involved in the pathogenesis of RA should open up avenues for developing radical **treatment** strategies directed at the cause of the disease. The Association de Recherche sur la Polyarthrite (ARP) supports research in this field, in which our group has been involved since 1993. Thanks to this support, considerable progress has been made. Several combinations of susceptibility alleles of various genes are probably involved in the development of RA. Although HLA-DRB1 is the main RA gene, it accounts for only part of the familial risk for RA. HLA-DRB1 alleles are neither necessary nor sufficient to cause the development of RA in a given individual. Several genome scans conducted in populations from France, Japan, North America and UK have confirmed the role of the HLA region and suggested several other susceptibility loci. Association studies support a role for several genes, including TNFR2, PADI4, SLC22A4, RUNX1, and PTPN22. However, the imperfect matching of cases and controls requires that confirmation of these results be obtained. To confirm that a gene confers susceptibility to RA, the association must be replicated in several independent studies and, more importantly, evidence of genetic linkage must be obtained in family studies. The identification of genetic factors conferring susceptibility to RA will open up new avenues toward radical **treatments** for RA and may help to optimize the diagnostic, prognostic, and pharmacogenetic management of today's patients with RA. .COPYRGT. 2005 Elsevier SAS. All rights reserved.

L25 ANSWER 11 OF 28 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN
ACCESSION NUMBER: 2006:6150 BIOSIS
DOCUMENT NUMBER: PREV200600003663
TITLE: Methotrexate reduces protein citrullination in vitro: A possible explanation for its singular in vivo effectiveness in **rheumatoid** arthritis.
AUTHOR(S): Menard, Henri A. [Reprint Author]; Lora, Maximilien; Zhou, ZhiJie
CORPORATE SOURCE: McGill Univ, Montreal, PQ, Canada
SOURCE: Arthritis & Rheumatism, (SEP 2005) Vol. 52, No. 9, Suppl. S, pp. S355.
Meeting Info.: 69th Annual Scientific Meeting of the American-College-of-Rheumatology/40th Annual Scientific Meeting of the Association-of-Rheumatology-Health-Professionals. San Diego, CA, USA. November 12 -17, 2005. Amer Coll Rheumatol; Assoc Rheumatol Hlth Profess.
CODEN: ARHEAW. ISSN: 0004-3591.
DOCUMENT TYPE: Conference; (Meeting)
Conference; (Meeting Poster)
LANGUAGE: English
ENTRY DATE: Entered STN: 14 Dec 2005
Last Updated on STN: 14 Dec 2005

L25 ANSWER 12 OF 28 EMBASE COPYRIGHT (c) 2006 Elsevier B.V. All rights reserved on STN
ACCESSION NUMBER: 2005163655 EMBASE

TITLE: From animal models to human genetics: Research on the induction and pathogenicity of autoantibodies.
AUTHOR: Conrad K.; Bachmann M.P.; Matsuura E.; Shoenfeld Y.
CORPORATE SOURCE: K. Conrad, Institute for Immunology, Medical Faculty, Technical University Dresden, Fetscherstrasse 74, D-01307 Dresden, Germany. k_conrad@rcs.urz.tu-dresden.de
SOURCE: Autoimmunity Reviews, (2005) Vol. 4, No. 3, pp. 178-187. .
Refs: 1
ISSN: 1568-9972 CODEN: ARUEBU
COUNTRY: Netherlands
DOCUMENT TYPE: Journal; Conference Article
FILE SEGMENT: 005 General Pathology and Pathological Anatomy
022 Human Genetics
026 Immunology, Serology and Transplantation
027 Biophysics, Bioengineering and Medical Instrumentation
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 20050602
Last Updated on STN: 20050602 .

AB The revolutionary techniques of modern molecular and cellular biology enhance almost daily our knowledge of immunity and autoimmunity in men and experimental animals. Our fragmentary puzzle of the immune system is going to form a fascinating picture of a masterpiece of evolution. Although many of these aspects were achieved by analysis of human body fluids and tissues, the etiopathogenesis of autoimmune diseases cannot readily be analyzed without appropriate animal models. Therefore, the 7th Dresden Symposium on Autoantibodies has focused on experimental autoimmune models. The 295 attendants of the symposium listened to and discussed about the pathogenesis and **therapy** of autoimmunity in experimental mouse models, natural and pathogenic autoantibodies, molecular mechanisms of xenobiotic-induced autoimmunity, the genetic background of autoimmune diseases, novel autoantibodies and their pathogenic and/or clinical relevance, autoantibodies in systemic and neurological diseases, the occurrence and measurement of **therapy**-induced antibodies and methodical aspects as well as novel diagnostic strategies including multiplex assays for autoantibody profiling. Those who are interested to read the full length articles are referred to the book published in parallel to this meeting ([Conrad K, Bachmann MP, Chan EKL, Fritzler MJ, Humbel RL, Sack U, Shoenfeld Y, editors. From animal models to human genetics: research on the induction and pathogenicity of autoantibodies, Report on the 7th Dresden Symposium on Autoantibodies held in Dresden on September 1-4, 2004. Germany: Pabst Science Publishers; 2004.]; www.pabst-publishers.de). .COPYRGT. 2004 Elsevier B.V. All rights reserved.

L25 ANSWER 13 OF 28 SCISEARCH COPYRIGHT (c) 2006 The Thomson Corporation on STN
ACCESSION NUMBER: 2005:1208620 SCISEARCH
THE GENUINE ARTICLE: 990HY
TITLE: Almost all about citrulline in mammals
AUTHOR: Curis E (Reprint); Nicolis I; Moinard C; Osowska S; Zerrouk N; Benazeth S; Cynober L
CORPORATE SOURCE: Univ Paris 05, Fac Pharm, Lab Biomath, EA 2498, 4 Ave Observ, F-75006 Paris, France (Reprint); Univ Paris 05, Fac Pharm, Lab Biomath, EA 2498, F-75006 Paris,

France; Univ Paris 05, Fac Pharm, Lab Biol Nutr, EA 2498, F-75006 Paris, France; Univ Paris 05, Fac Pharm, Lab Pharmacotech, EA 2498, F-75006 Paris, France; Assistance Publ Hop Paris, Hotel Dieu, Biochim Lab, Paris, France
emmanuel.curis@univ-paris5.fr
COUNTRY OF AUTHOR: France
SOURCE: AMINO ACIDS, (NOV 2005) Vol. 29, No. 3, pp. 177-205. ISSN: 0939-4451.
PUBLISHER: SPRINGER, 233 SPRING STREET, NEW YORK, NY 10013 USA.
DOCUMENT TYPE: General Review; Journal
LANGUAGE: English
REFERENCE COUNT: 199
ENTRY DATE: Entered STN: 15 Dec 2005
Last Updated on STN: 15 Dec 2005
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB Citrulline (Cit, C6H13N3O3), which is a ubiquitous amino acid in mammals, is strongly related to arginine. Citrulline metabolism in mammals is divided into two fields: free citrulline and citrullinated proteins. Free citrulline metabolism involves three key enzymes: NO synthase (NOS) and ornithine carbamoyltransferase (OCT) which produce citrulline, and argininosuccinate synthetase (ASS) that converts it into argininosuccinate. The tissue distribution of these enzymes distinguishes three "orthogonal" metabolic pathways for citrulline. Firstly, in the liver, citrulline is locally synthesized by OCT and metabolized by ASS for urea production. Secondly, in most of the tissues producing NO, citrulline is recycled into arginine via ASS to increase arginine availability for NO production. Thirdly, citrulline is synthesized in the gut from glutamine (with OCT), released into the blood and converted back into arginine in the kidneys (by ASS); in this pathway, circulating citrulline is in fact a masked form of arginine to avoid liver captation. Each of these pathways has related pathologies and, even more interestingly, citrulline could potentially be used to monitor or **treat** some of these pathologies. Citrulline has long been administered in the **treatment** of inherited urea cycle disorders, and recent studies suggest that citrulline may be used to control the production of NO. Recently, citrulline was demonstrated as a potentially useful marker of short bowel function in a wide range of pathologies. One of the most promising research directions deals with the administration of citrulline as a more efficient alternative to arginine, especially against underlying splanchnic sequestration of amino acids. Protein citrullination results from post-translational modification of arginine; that occurs mainly in keratinization-related proteins and myelins, and insufficiencies in this citrullination occur in some auto-immune diseases such as **rheumatoid** arthritis, psoriasis or multiple sclerosis.

L25 ANSWER 14 OF 28 JICST-EPlus COPYRIGHT 2006 JST on STN
ACCESSION NUMBER: 1050502888 JICST-EPlus
TITLE: Studies of preparation of **treatment** plan of articular rheumatism by new biologics and its verification. Study of development of the new anti-citrulline peptide antibody assay system and development as a biologics reaction predictor.
AUTHOR: SAWADA TETSUJI
CORPORATE SOURCE: Fac. Medicine, Univ. Tokyo, JPN
SOURCE: Kansetsu Riumachi Chiryo ni okeru Shinki Seibutsu Seizai no Chiryo Hoshin no Sakusei oyobi sono Kensho ni

kansuru Kenkyu Heisei 16 Nendo Sokatsu, Buntan Kenkyu Hokokusho, (2005) pp. 32-34. Journal Code: N20051319 (Fig. 3)
PUB. COUNTRY: Japan
DOCUMENT TYPE: Journal; Article
LANGUAGE: Japanese
STATUS: New

AB A new anti-citrulline peptide antibody assay system was prepared, and the relation between antibody formation and PADI (**peptidyl arginine deiminases**) gene polymorphism was examined. This time, preparation of the assay system using the soluble fraction of synovial cells as an antigen was attempted, The anti-citrulline peptide antibody activity was detected in the partial articular rheumatism (RA) patient's serum by ELISA. For the Western blot using the Senshu antibody, many bands of citrulline protein were detected in the PADI-**treated** synovial cell protein. However, the bands recognized in the RA patient's serum was only a part of the bands among them, and were different depending on patient.

L25 ANSWER 15 OF 28 EMBASE

ACCESSION NUMBER: 2005170772 EMBASE
TITLE: Autoantibodies to citrullinated proteins: ACPA.
AUTHOR: Vincent C.; Nogueire L.; Clavel C.; Sebbag M.; Serre G.
CORPORATE SOURCE: G. Serre, U. Diff. Epidermique Autoimmunite, UMR 5165 CNRS-UPS, Hopital Purpan, Place du Dr Baylac, 31059 Toulouse Cedex, France. serre.sec@chu-toulouse.fr
SOURCE: Autoimmunity, (2005) Vol. 38, No. 1, pp. 17-24. .
Refs: 57
ISSN: 0891-6934 CODEN: AUIMEI
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 005 General Pathology and Pathological Anatomy
026 Immunology, Serology and Transplantation
029 Clinical Biochemistry
031 Arthritis and Rheumatism
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 20050505
Last Updated on STN: 20050505

AB Anti-perinuclear factor and anti-keratin antibodies have long been known to be specifically associated with **rheumatoid arthritis** (**RA**). They were first demonstrated to target various forms of (pro)filaggrin, a protein of stratified epithelia. Then, they were found to belong to a single family of autoantibodies targeting proteins that bear peptidic epitopes centered by a citrullyl residue: the anti-citrullinated protein autoantibodies (ACPA). The main targets of ACPA in the synovial tissue were demonstrated to be citrullinated forms of the α- and β-chains of fibrin. A chronic conflict between locally produced ACPA and deposits of citrullinated fibrin is probably responsible for self-maintaining of RA synovial inflammation. Various tests for the detection of ACPA have been developed: recent ELISAs confirm their high diagnostic specificity and improve their diagnostic sensitivity. Since ACPA appear very early in the course of the disease, their detection is of major interest to identify RA among recent arthritides. Moreover, their prognostic value may lead to start early 'aggressive' **treatments** to **prevent** irreversible joint damage. .COPYRGT. 2005 Taylor & Francis Ltd.

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ACCESSION NUMBER: 2005068726 EMBASE
TITLE: The role of B cells in the pathogenesis of **rheumatoid** arthritis.
AUTHOR: Kotzin B.L.
CORPORATE SOURCE: Dr. B.L. Kotzin, Amgen, Inc., One Amgen Center Drive, Thousand Oaks, CA 91320, United States. bkotzin@amgen.com
SOURCE: Journal of Rheumatology, (2005) Vol. 32, No. SUPPL. 73, pp. 14-18. .
Refs: 33
ISSN: 0315-162X CODEN: JRHUA
COUNTRY: Canada
DOCUMENT TYPE: Journal; Conference Article
FILE SEGMENT: 005 General Pathology and Pathological Anatomy
022 Human Genetics
026 Immunology, Serology and Transplantation
031 Arthritis and Rheumatism
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 20050224
Last Updated on STN: 20050224

AB The classical paradigm for **rheumatoid arthritis** (**RA**) pathogenesis holds that CD4+ T cells mediate joint damage both directly and by driving non-T effector cells to release inflammatory cytokines. By contrast, the new paradigm that is developing centers on an interaction of CD4+ T cells with B cells. Evidence reviewed in this article shows that autoreactive B cells can be driven by the T cells to produce IgG autoantibodies that may be directly involved in joint damage, and B cells are known to be critical in activating CD4+ T cells. As the B cell appears to play an important role in the RA process, it is appropriate to consider how B cell-mediated effects might be reduced or **prevented** in patients with this disease. As the targeted depletion of B cells with a monoclonal antibody such as rituximab appears to be clinically effective in RA patients, this approach shows great **therapeutic** potential.

L25 ANSWER 17 OF 28 MEDLINE on STN

ACCESSION NUMBER: 2004385733 MEDLINE
DOCUMENT NUMBER: PubMed ID: 15290721
TITLE: The joy of citrulline: new insights into the diagnosis, pathogenesis, and **treatment** of **rheumatoid** arthritis.
AUTHOR: Hill Jonathan; Cairns Ewa; Bell David A
SOURCE: The Journal of rheumatology, (2004 Aug) Vol. 31, No. 8, pp. 1471-3. Ref: 18
Journal code: 7501984. ISSN: 0315-162X.
PUB. COUNTRY: Canada
DOCUMENT TYPE: Editorial
General Review; (REVIEW)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200411
ENTRY DATE: Entered STN: 20040804
Last Updated on STN: 20041219

Searcher : Shears 571-272-2528

Entered Medline: 20041129

L25 ANSWER 18 OF 28 WPIDS COPYRIGHT 2006 THE THOMSON CORP on STN
ACCESSION NUMBER: 2004-710426 [70] WPIDS
DOC. NO. NON-CPI: N2004-563380
DOC. NO. CPI: C2004-250584
TITLE: Novel citrullinated antigenic peptides for diagnosing **rheumatoid** arthritis, binds with high affinity to major histocompatibility complex class II molecule having shared epitope and evokes T cell response in autoimmune disorder patients.
DERWENT CLASS: B04 D16 S03
INVENTOR(S): BELL, D; CAIRNS, E; HILL, J
PATENT ASSIGNEE(S): (LONH-N) LONDON HEALTH SCI CENT RES INC
COUNTRY COUNT: 1
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
CA 2421321	A1	20040907	(200470)*	EN	62

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
CA 2421321	A1	CA 2003-2421321	20030307

PRIORITY APPLN. INFO: CA 2003-2421321 20030307
AN 2004-710426 [70] WPIDS
AB CA 2421321 A UPAB: 20041101
NOVELTY - A citrullinated peptide (I) binding with a high or increased affinity to a major histocompatibility complex (MHC) class II molecule having the shared epitope, where the binding to the shared epitope evokes a T cell response in the blood of a patient with an autoimmune disorder, is new.

DETAILED DESCRIPTION - A citrullinated peptide (I) binding with a high or increased affinity to a major histocompatibility complex (MHC) class II molecule having the shared epitope, where the binding to the shared epitope evokes a T cell response in the blood of a patient with an autoimmune disorder, and comprises any one of the 37 amino acid sequences (S1)-(S37), given in the specification e.g. Ser-Ala-Val-Arg-Ala-Cit-Ser-Ser-Val-Pro-Gly-Val-Arg, Phe-Gln-Lys-Cit-Leu-Asp-Gly-Ser-Val, Tyr-Ala-Leu-Cit-Val-Glu-Leu-Glu-Asp, Val-Glu-Thr-Cit-Asp-Gly-Gln-Val-Ile and their functional analogs.

INDEPENDENT CLAIMS are also included for the following:

(1) a pharmaceutical composition comprising (I) and a carrier;

(2) making (I);

(3) a test kit for the detection of activated autoreactive T cells which are reactive with a citrullinated peptide antigen bound to a major histocompatibility complex (MHC) class II shared epitope positive cell, comprising (I);

(4) **treating** (M1) a subject suffering from **rheumatoid** arthritis evoked by the binding of a citrullinated peptide to MHC class II molecule with the shared epitope leading to T cell activation and an inflammatory response, by administering a T cell tolerance inducing amount of a composition comprising (I) and a carrier;

(5) a diagnostic method (M2) for autoimmune disorders involving

the formation of citrullinated antigen MHC class II with the shared epitope cell complexes, involves incubating an isolated sample of peripheral blood mononuclear cells from a subject with one or more citrullinated peptide antigens, detecting the formation of citrullinated antigen MHC class II with the shared epitope cell complexes, such detection indicating a likelihood of evoking a T cell response leading to an autoimmune disorder in the subject;

(6) minimizing or **preventing** the activation of T cells by a citrullinated peptide MHC class II having a shared epitope complex in a subject, involves administering antibodies targeted to the complex to the subject;

(7) **preventing** the conversion of arginine to citrulline in a potentially antigenic peptide in a subject, involves administering an antagonist or inhibitor of **peptidylarginine deiminase** to the subject;

(8) screening method to identify pharmaceutical compounds that inhibit binding of a citrullinated peptide to a MHC class II molecule having a shared epitope, involves administering to a transgenic DR4-IE tg mouse a candidate pharmaceutical compound, and measuring T cell activity and/or measuring citrullinated peptide/MHC class II molecule with a shared epitope complex formation; and

(9) inducing (M3) **rheumatoid** arthritis in an animal to provide an animal model for the study of **rheumatoid** arthritis, involves administering to the animal a **rheumatoid** arthritis inducing amount of a composition comprising (I) with a carrier.

ACTIVITY - **Antiarthritic; Antirheumatic.**

MECHANISM OF ACTION - Inhibitor of binding of citrullinated antigenic peptides to MHC class II molecule.

No biological data is given.

USE - (I) is useful for **treating** a subject with **rheumatoid** arthritis, which involves interfering with the binding of (I) to the MHC class II molecule having a shared epitope in the subject. (I) is useful for diagnosing **rheumatoid** arthritis, which involves contacting a blood sample from a subject with (I) or its functional analogue, and determining whether T cells in the sample are activated and/or determining whether a complex is formed between (I) and the MHC class II molecule having a shared epitope. (I) is useful for diagnosing **rheumatoid** arthritis, or susceptibility to **rheumatoid** arthritis in a subject, which involves determining if T cells of the subject recognize (I) bound to a MHC class II molecule having a shared epitope on an antigen presenting cell of the subject, where recognition by the T cells indicates that the subject has, or is susceptible to, **rheumatoid** arthritis. (I) is also useful in a diagnostic method for the detection of autoreactive T cells which are reactive with a citrullinated peptide antigen bound to an MHC class II molecule having a shared epitope, which involves incubating an isolated sample of peripheral blood mononuclear cells from a subject with (I), and detecting the response of CD4+T cells, indicating the presence of activated autoreactive T cells in the subject. The activated T cells indicate that the subject has, or is susceptible to an autoimmune disorder. (M1) is useful for **treating rheumatoid** arthritis. (M2) is useful for diagnosing autoimmune disorder such as **rheumatoid** arthritis. (I) and (M3) is useful for inducing **rheumatoid** arthritis in an animal to provide an animal model. (All claimed.)

DESCRIPTION OF DRAWING(S) - The figure is a graph showing T cell immune response in DR4-1E tg mice to peptides containing arginine,

citrulline or aspartic acid at the position that interacts with the P4 pocket formed by the shared epitope.
Dwg.1/3

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ACCESSION NUMBER: 2004330466 EMBASE
TITLE: The joy of citrulline: New insights into the diagnosis, pathogenesis, and **treatment** of **rheumatoid** arthritis.
AUTHOR: Hill J.; Cairns E.; Bell D.A.
CORPORATE SOURCE: Dr. D.A. Bell, Rheumatology Centre, Monsignor Roney Building, St. Joseph's Health Centre, 268 Grosvenor Street, London, Ont. N6A 4V2. david.bell@sjhc.london.on.ca
SOURCE: Journal of Rheumatology, (2004) Vol. 31, No. 8, pp. 1471-1473. .
Refs: 18
ISSN: 0315-162X CODEN: JRHUA
COUNTRY: Canada
DOCUMENT TYPE: Journal; Editorial
FILE SEGMENT: 005 General Pathology and Pathological Anatomy
026 Immunology, Serology and Transplantation
031 Arthritis and Rheumatism
LANGUAGE: English
ENTRY DATE: Entered STN: 20040826
Last Updated on STN: 20040826

DATA NOT AVAILABLE FOR THIS ACCESSION NUMBER

L25 ANSWER 20 OF 28 MEDLINE on STN DUPLICATE 4

ACCESSION NUMBER: 2004377481 MEDLINE
DOCUMENT NUMBER: PubMed ID: 15247907
TITLE: Structural basis for Ca(2+)-induced activation of human PAD4.
AUTHOR: Arita Kyouhei; Hashimoto Hiroshi; Shimizu Toshiyuki; Nakashima Katsuhiko; Yamada Michiyuki; Sato Mamoru
CORPORATE SOURCE: Graduate School of Integrated Science, Yokohama City University, 1-7-29 Suehiro-cho, Tsurumi-ku, Yokohama 230-0045, Japan.
SOURCE: Nature structural & molecular biology, (2004 Aug) Vol. 11, No. 8, pp. 777-83. Electronic Publication: 2004-07-11.
Journal code: 101186374. ISSN: 1545-9993.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
OTHER SOURCE: PDB-1WD8; PDB-1WD9; PDB-1WDA
ENTRY MONTH: 200409
ENTRY DATE: Entered STN: 20040729
Last Updated on STN: 20040917
Entered Medline: 20040916

AB **Peptidylarginine deiminase** 4 (PAD4) is a Ca(2+)-dependent enzyme that catalyzes the conversion of protein arginine residues to citrulline. Its gene is a susceptibility locus for **rheumatoid** arthritis. Here we present the crystal structure of Ca(2+)-free wild-type PAD4, which shows that the polypeptide chain adopts an elongated fold in which the N-terminal domain forms two immunoglobulin-like subdomains, and the C-terminal

domain forms an alpha/beta propeller structure. Five Ca(2+)-binding sites, none of which adopt an EF-hand motif, were identified in the structure of a Ca(2+)-bound inactive mutant with and without bound substrate. These structural data indicate that Ca(2+) binding induces conformational changes that generate the active site cleft. Our findings identify a novel mechanism for enzyme activation by Ca(2+) ions, and are important for understanding the mechanism of protein citrullination and for developing PAD-inhibiting drugs for the **treatment** of **rheumatoid** arthritis.

L25 ANSWER 21 OF 28 MEDLINE on STN DUPLICATE 5
ACCESSION NUMBER: 2004618535 MEDLINE
DOCUMENT NUMBER: PubMed ID: 15589429
TITLE: Clinical and pathophysiological significance of the autoimmune response to citrullinated proteins in **rheumatoid** arthritis.
AUTHOR: Sebbag Mireille; Chapuy-Regaud Sabine; Auger Isabelle; Petit-Texeira Elisabeth; Clavel Cyril; Nogueira Leonor; Vincent Christian; Cornelis Francois; Roudier Jean; Serre Guy
CORPORATE SOURCE: Faculte de Medecine, Purpan-IFR30, Unite Differenciation Epidermique et Auto-immunite Rhumatoide, UMR 5165 CNRS-Toulouse III Universite, (CNRS-Inserm-Universite Paul Sabatier-CHU de Toulouse), Place du Docteur Baylac, 31059 Toulouse, France.
SOURCE: Joint, bone, spine : revue du rhumatisme, (2004 Nov) Vol. 71, No. 6, pp. 493-502. Ref: 100
Journal code: 100938016. ISSN: 1297-319X.
PUB. COUNTRY: France
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200503
ENTRY DATE: Entered STN: 20041220
Last Updated on STN: 20050305
Entered Medline: 20050304

AB **Rheumatoid arthritis** (**RA**) is the most frequent human autoimmune disease, affecting about 1% of the adult population worldwide. A better knowledge of the autoimmune mechanisms involved is essential. We identified the epithelial targets of various autoantibodies specifically associated to RA, as variants of (pro)filaggrin. We also showed that these targets correspond to deiminated ("citrullinated") proteins, of which arginyl residues have been posttranslationally transformed into citrullyl residues by a **peptidylarginine deiminase** (**PAD**).
Moreover, we and others established that citrullyl residues are indispensable elements of the epitopes recognized by these autoantibodies but only in the context of specific aminoacid sequences. We also demonstrated that these autoantibodies to citrullinated proteins (ACPA) are secreted by plasma cells of the synovial tissue and that their major targets correspond to citrullinated forms of the alpha- and beta-chains of fibrin, abundant in the tissue. These results have allowed the development of new efficient immunochemical methods for the detection of ACPA. Some of them are already commercially available. These new methods have permitted the high diagnostic value of ACPA which are present very early in the course of the disease, and also their prognostic value, to be confirmed. ACPA detection should therefore prove to be also a

very valuable tool to guide the choice of **therapeutic** strategies, from the earliest stages of the disease. The synthesis of ACPA in the **rheumatoid** synovial tissue and the existence therein of a specific antigenic target constitute a strong argument for the involvement of this specific immunological conflict in the pathophysiology of RA. Indeed, it could lead to activation of effector mechanisms with pro-inflammatory effects, thus to formation in the tissue of new fibrin deposits, secondarily citrullinated. We therefore, propose a new pathophysiological model accounting for the self-maintenance and chronicity of **rheumatoid** inflammation. Numerous questions about the pathophysiological significance of the autoimmune response to deiminated proteins in RA remain to be answered to confirm this model.

L25 ANSWER 22 OF 28 MEDLINE on STN DUPLICATE 6
ACCESSION NUMBER: 2004419394 MEDLINE
DOCUMENT NUMBER: PubMed ID: 15324932
TITLE: Influence of arginine deimination on antigenicity of fibrinogen.
AUTHOR: Hida Shunsuke; Miura Noriko N; Adachi Yoshiyuki; Ohno Naohito
CORPORATE SOURCE: Laboratory for Immunopharmacology of Microbial Products, School of Pharmacy, Tokyo University of Pharmacy and Life Science, 1432-1 Horinouchi, Hachioji, Tokyo 192-0392, Japan.
SOURCE: Journal of autoimmunity, (2004 Sep) Vol. 23, No. 2, pp. 141-50.
Journal code: 8812164. ISSN: 0896-8411.
PUB. COUNTRY: England: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200504
ENTRY DATE: Entered STN: 20040825
Last Updated on STN: 20050420
Entered Medline: 20050419

AB Autoreactivity is controlled at various steps by numerous mechanisms and is a key to understanding and **treating** autoimmune disease. Recently, an antibody against deiminated fibrinogen (DI-FBG) was detected in patients with **rheumatoid arthritis** (**RA**) with high specificity and sensitivity. DI-FBG converted enzymically by **peptidyl arginine deiminase**, was also detected in synovial membrane. In the present study, we investigated whether antibody to DI-FBG is produced in mice immunized with DI-FBG. Mice were immunized with DI-FBG in the presence or absence of adjuvant. Production of the specific antibody was only induced with adjuvant. The resulting antibody was specific for DI-FBG and did not react with intact/native fibrinogen. Furthermore, it recognized deiminated human fibrinogen and cyclic citrullinated peptide (CCP). These results suggested that mouse fibrinogen acquires antigenicity in mice through deimination and therefore, autoantibody such as that detected in RA patients specifically may be induced.

L25 ANSWER 23 OF 28 MEDLINE on STN DUPLICATE 7
ACCESSION NUMBER: 2004558512 MEDLINE
DOCUMENT NUMBER: PubMed ID: 15530456
TITLE: Autoantibodies to citrullinated proteins in **rheumatoid arthritis**: clinical

performance and biochemical aspects of an **RA** -specific marker.
AUTHOR: Nijenhuis Suzanne; Zendman Albert J W; Vossenaar Erik R; Pruijn Ger J M; vanVenrooij Walther J
CORPORATE SOURCE: Department of Biochemistry 161, Radboud University Nijmegen, PO Box 9101, NL-6500 HB Nijmegen, The Netherlands.
SOURCE: Clinica chimica acta; international journal of clinical chemistry, (2004 Dec) Vol. 350, No. 1-2, pp. 17-34. Ref: 138
Journal code: 1302422. ISSN: 0009-8981.
PUB. COUNTRY: Netherlands
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200504
ENTRY DATE: Entered STN: 20041109
Last Updated on STN: 20050426
Entered Medline: 20050425

AB **Rheumatoid arthritis** (**RA**) is a common, systemic autoimmune disease of which the exact etiology is not known. In the past 10 years, substantial progress has been made in the identification of the antigens specifically recognized by the autoantibodies of RA patients. A central factor in this respect is citrullination, a form of post-translational modification that is strongly associated with autoimmunity in RA. Here, we summarize and discuss our current knowledge on (i) autoantibody systems in RA, (ii) the occurrence of **peptidylarginine deiminases** and (iii) citrullinated proteins in natural and diseased environments, and (iv) genetic factors involved in RA that may influence the generation and presentation of citrullinated proteins and the resulting antibody production against these modified proteins. Citrullination of proteins may play a key role in the initiation and/or the progression of RA. The onset of citrulline-specific autoimmunity in RA is probably mediated by both environmental and genetic factors, and future studies will learn whether **therapeutic** intervention at the level of citrullination may provide new possibilities to **treat** RA.

L25 ANSWER 24 OF 28 MEDLINE on STN
ACCESSION NUMBER: 2003178343 MEDLINE
DOCUMENT NUMBER: PubMed ID: 12696470
TITLE: Anti-cyclic citrullinated peptide antibodies as a diagnostic test for **rheumatoid** arthritis.
AUTHOR: Orbach Hedi; Shoenfeld Yehuda
SOURCE: Harefuah, (2003 Mar) Vol. 142, No. 3, pp. 182-5, 239.
Journal code: 0034351. ISSN: 0017-7768.
PUB. COUNTRY: Israel
DOCUMENT TYPE: Editorial
LANGUAGE: Hebrew
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200305
ENTRY DATE: Entered STN: 20030417
Last Updated on STN: 20030514
Entered Medline: 20030513

AB Early diagnosis of **rheumatoid arthritis** (**RA**) is important since aggressive **therapy** should begin at an early stage. Diagnosis is made on a clinical basis,

supported by the determination of **rheumatoid** factor (RF). However, RF is also positive in healthy subjects, as well as in other autoimmune and infectious diseases. Two other diagnostic markers with a high specificity for RA, antiperinuclear factor (APF) and antikeratin antibodies (AKA), are not in general use because of technical difficulties. APF and AKA are antifilaggrin antibodies (AFA) that bind to determinants rich in the unusual amino acid citrulline, generated by posttranscriptional modification of arginine residues by the enzyme **peptidylarginine deiminase** (**PAD**). Enzymatic determination of recombinant filaggrin fragments produces linear peptides, which are recognized by RA-specific autoantibodies. After substitution of serine by cysteine, a cyclic peptide is formed. The conformational change mimics the original structure of the filaggrin and enhances the affinity of the antibodies. Recently, an anti-cyclic citrullinated peptide (anti-CCP) ELISA was developed. The sensitivity of this test is usually 51%-68%, with a specificity of about 96%-98% (significantly higher than that of RF). Together with RF, anti-CCP increases the ability to diagnose patients with early RA. The test might help to predict which patients will develop persistent disease with evidence of radiologic lesions. Implementation of the highly specific anti-CCP test in conjunction with RF would enable reliable early diagnosis in some cases and allow the initiation of aggressive **therapy** with disease modifying anti-rheumatic drugs (DMARDs).

L25 ANSWER 25 OF 28 EMBASE

ACCESSION NUMBER: 2003150637 EMBASE
TITLE: Anti-cyclic citrullinated peptide antibodies as a diagnostic test for **rheumatoid** arthritis.
AUTHOR: Orbach H.; Shoenfeld Y.
CORPORATE SOURCE: H. Orbach, Department of Internal Medicine, Rheumatology Unit, Bikur Cholim Hospital, Jerusalem, Israel
SOURCE: Harefuah, (1 Mar 2003) Vol. 142, No. 3, pp. 182-185+239. .
Refs: 34
ISSN: 0017-7768 CODEN: HAREA6
COUNTRY: Israel
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 026 Immunology, Serology and Transplantation
029 Clinical Biochemistry
031 Arthritis and Rheumatism
LANGUAGE: Hebrew
SUMMARY LANGUAGE: English; Hebrew
ENTRY DATE: Entered STN: 20030424
Last Updated on STN: 20030424

AB Early diagnosis of **rheumatoid arthritis** (**RA**) is important since aggressive **therapy** should begin at an early stage. Diagnosis is made on a clinical basis, supported by the determination of **rheumatoid** factor (RF). However, RF is also positive in healthy subjects, as well as in other autoimmune and infectious diseases. Two other diagnostic markers with a high specificity for RA, antiperinuclear factor (APF) and antikeratin antibodies (AKA), are not in general use because of technical difficulties. APF and AKA are antifilaggrin antibodies (AFA) that bind to determinants rich in the unusual amino acid citrulline, generated by posttranscriptional modification of arginine residues by the enzyme **peptidylarginine deiminase**

(**PAD**). Enzymatic deimination of recombinant filaggrin fragments produces linear peptides, which are recognized by RA-specific autoantibodies. After substitution of serine by cysteine, a cyclic peptide is formed. The conformational change mimics the original structure of the filaggrin and enhances the affinity of the antibodies. Recently, an anti-cyclic citrullinated peptide (anti-CCP) ELISA was developed. The sensitivity of this test is usually 51%-68%, with a specificity of about 96%-98% (significantly higher than that of RF). Together with RF, anti-CCP increases the ability to diagnose patients with early RA. The test might help to predict which patients will develop persistent disease with evidence of radiologic lesions. Implementation of the highly specific anti-CCP test in conjunction with RF would enable reliable early diagnosis in some cases and allow the initiation of aggressive **therapy** with disease modifying anti-rheumatic drugs (DMARDs).

L25 ANSWER 26 OF 28 WPIDS COPYRIGHT 2006 THE THOMSON CORP on STN
ACCESSION NUMBER: 2001-114394 [13] WPIDS
DOC. NO. NON-CPI: N2001-084087
DOC. NO. CPI: C2001-034134
TITLE: New citrulline-containing polypeptide from fibrin, useful for diagnosis and **treatment** of **rheumatoid** polyarthritis.
DERWENT CLASS: B04 D16 S03
INVENTOR(S): SEBBAG, M; SERRE, G
PATENT ASSIGNEE(S): (UYTO-N) UNIV TOULOUSE SABATIER PAUL; (INMR) BIOMERIEUX SA
COUNTRY COUNT: 22
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
FR 2795735	A1	20010105	(200113)*		23
WO 2001002437	A1	20010111	(200113)	FR	
RW: AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE					
W: CA JP US					
EP 1196450	A1	20020417	(200233)	FR	
R: AT BE CH CY DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE					
JP 2003504314	W	20030204	(200320)		23
EP 1196450	B1	20051116	(200579)	FR	
R: AT BE CH CY DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE					
DE 60024092	E	20051222	(200603)		
EP 1619205	A1	20060125	(200608)	FR	
R: AT BE CH CY DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE					

APPLICATION DETAILS:

PATENT NO	KIND		APPLICATION	DATE
FR 2795735	A1		FR 1999-8470	19990701
WO 2001002437	A1		WO 2000-FR1857	20000630
EP 1196450	A1		EP 2000-949595	20000630
			WO 2000-FR1857	20000630
JP 2003504314	W		WO 2000-FR1857	20000630
			JP 2001-508224	20000630
EP 1196450	B1		EP 2000-949595	20000630
			WO 2000-FR1857	20000630
		Related to	EP 2005-20523	20050921
DE 60024092	E		DE 2000-00024092	20000630

Searcher : Shears 571-272-2528

		EP 2000-949595	20000630
		WO 2000-FR1857	20000630
EP 1619205	A1 Div ex	EP 2000-949595	20000630
		EP 2005-20523	20000630

FILING DETAILS:

PATENT NO	KIND	PATENT NO
EP 1196450	A1 Based on	WO 2001002437
JP 2003504314	W Based on	WO 2001002437
EP 1196450	B1 Based on	WO 2001002437
DE 60024092	E Based on	EP 1196450
	Based on	WO 2001002437
EP 1619205	A1 Div ex	EP 1196450

PRIORITY APPLN. INFO: FR 1999-8470 19990701
AN 2001-114394 [13] WPIDS
AB FR 2795735 A UPAB: 20010307
NOVELTY - Citrulline (Cit) containing polypeptide (I) derived from all or part of the alpha - or beta -chains of fibrin (from a vertebrate) by substitution of at least one arginine residue by Cit, is new.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:

(1) antigenic composition for detecting autoantibodies (AAb) specific for **rheumatoid** polyarthritis (RP), comprising at least one (I), optionally labeled and/or conjugated to a carrier protein;

(2) method for detecting AAb;

(3) kit for detecting AAb; and

(4) pharmaceutical composition containing at least one (I) as active ingredient.

ACTIVITY - Anti-arthritic; anti-inflammatory.

No biological data is given.

MECHANISM OF ACTION - Neutralization of an autoimmune response, especially inhibition of fixation of humoral/cellular effectors of the response. The antigen responsible for the autoimmune response in **rheumatoid** polyarthritis has been identified as citrulline-containing derivatives of fibrin chains.

USE - (I) are used for in vitro diagnosis of **rheumatoid** polyarthritis (RP), by detecting disease-specific autoantibodies, and **therapeutically** for neutralizing the RP-associated autoimmune response.

ADVANTAGE - (I) can detect autoantibodies associated with **rheumatoid** polyarthritis in serum with high sensitivity.

Dwg.0/3

L25 ANSWER 27 OF 28 WPIDS COPYRIGHT 2006 THE THOMSON CORP on STN
ACCESSION NUMBER: 1999-385357 [32] WPIDS
DOC. NO. NON-CPI: N1999-288616
DOC. NO. CPI: C1999-113336
TITLE: New peptide derived from intermediate filament proteins.
DERWENT CLASS: B04 D16 S03
INVENTOR(S): MEHEUS, L; RAYMACKERS, J; UNION, A
PATENT ASSIGNEE(S): (INNO-N) INNOGENETICS NV
COUNTRY COUNT: 84
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 9928344	A2	19990610	(199932)*	EN	73
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SZ UG ZW					
W: AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB GD GE GH GM HR HU ID IL IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT UA UG US UZ VN YU ZW					
AU 9921558	A	19990616	(199945)		
EP 949270	A1	19991013	(199947)	EN	
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI					
EP 1034186	A2	20000913	(200046)	EN	
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI					
HU 2000004338	A2	20010228	(200121)		
CZ 2000001963	A3	20020417	(200231)		
JP 2002512939	W	20020508	(200234)		78

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 9928344	A2	WO 1998-EP7714	19981130
AU 9921558	A	AU 1999-21558	19981130
EP 949270	A1	EP 1998-870078	19980409
EP 1034186	A2	EP 1998-965715	19981130
		WO 1998-EP7714	19981130
HU 2000004338	A2	WO 1998-EP7714	19981130
		HU 2000-4338	19981130
CZ 2000001963	A3	WO 1998-EP7714	19981130
		CZ 2000-1963	19981130
JP 2002512939	W	WO 1998-EP7714	19981130
		JP 2000-523235	19981130

FILING DETAILS:

PATENT NO	KIND		PATENT NO
AU 9921558	A	Based on	WO 9928344
EP 1034186	A2	Based on	WO 9928344
HU 2000004338	A2	Based on	WO 9928344
CZ 2000001963	A3	Based on	WO 9928344
JP 2002512939	W	Based on	WO 9928344.

PRIORITY APPLN. INFO: EP 1998-870078 19980409; EP 1997-870195 19971128

AN 1999-385357 [32] WPIDS

AB WO 9928344 A UPAB: 19991122

NOVELTY - (A) A novel peptide comprises a sequence of less than 50 amino acids of any variant of natural filaggrin or any variant of intermediate filament proteins is new.

DETAILED DESCRIPTION - (A) A novel peptide comprises a sequence of less than 50 amino acids of any variant of natural filaggrin or any variant of intermediate filament proteins, comprising at least one citrulline residue, and where the presence of the citrulline is crucial for reacting with antibodies that are present in sera from patients with **rheumatoid arthritis** (**RA**).

INDEPENDENT CLAIMS are also included for the following:

(1) an antibody specifically reactive with the citrulline residues of a peptide form as in (A) or specifically reactive with the citrulline residues of intermediate filament proteins, and with the antibody being preferably a monoclonal antibody (MAb);

(2) anti-idiotype antibody raised upon immunization with an antibody as in (1), with the anti-idiotype antibody being specifically reactive with an antibody as in (1), to mimic the peptide that contains citrulline as in (A), and with the antibody being preferably an MAb;

(3) an immunotoxin molecule comprising and/or consisting of cell recognition molecule being a peptide as in (A), or an antibody as in (1), to mimic the peptide that contains citrulline as in (A), and with the antibody being preferably a MAb;

(4) use of intermediate filament protein, preferably vimentin or cytokeratin 1 or cytokeratin 9, or antibodies raised upon immunization with intermediate filament proteins or a composition for the preparation of a **therapeutic** or of a diagnostic for RA;

(5) a diagnostic kit for use in detecting auto-immune diseases such as RA, systemic lupus erythematosus, discoid lupus erythematosus, scleroderma, dermatomyositis and Sjogren's syndrome, the kit comprising at least one peptide as in (A), or an antibody as in (1), or an intermediate filament protein, with the peptide, antibody or protein being optionally bound to a solid filament.

USE - The peptides constitute immunogenic determinants of antibodies present in patients with RA. The peptides, antibodies, immunotoxins and intermediate filament proteins can be used for the preparation of a **therapeutic** or of a diagnostic for RA (claimed). The peptides can also be used for identifying compounds which modulate the interaction between an autoantigen and a RA specific autoantibody. The products can also be used for the diagnosis and **treatment** of other autoimmune diseases e.g. systemic lupus erythematosus, discoid lupus erythematosus, scleroderma, dermatomyositis, or Sjogrens syndrome.

Dwg.0/7

L25 ANSWER 28 OF 28 MEDLINE on STN DUPLICATE 8

ACCESSION NUMBER: 1999101527 MEDLINE
DOCUMENT NUMBER: PubMed ID: 9886436
TITLE: The epitopes targeted by the **rheumatoid** arthritis-associated antifilaggrin autoantibodies are posttranslationally generated on various sites of (pro)filaggrin by deimination of arginine residues.
AUTHOR: Girbal-Neuhauser E; Durieux J J; Arnaud M; Dalbon P; Sebbag M; Vincent C; Simon M; Senshu T; Masson-Bessiere C; Jolivet-Reynaud C; Jolivet M; Serre G
CORPORATE SOURCE: Department of Biology and Pathology of the Cell, Institut National de la Sante et de la Recherche Medicale, Toulouse-Purpan School of Medicine, University Toulouse III, France.
SOURCE: Journal of immunology (Baltimore, Md. : 1950), (1999 Jan 1) Vol. 162, No. 1, pp. 585-94.
Journal code: 2985117R. ISSN: 0022-1767.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
OTHER SOURCE: GENBANK-AF043380
ENTRY MONTH: 199901

Searcher : Shears 571-272-2528

ENTRY DATE: Entered STN: 19990202
Last Updated on STN: 19990202
Entered Medline: 19990121

AB Antifilaggrin autoantibodies (AFA) are a population of IgG autoantibodies associated to **rheumatoid arthritis** (**RA**), which includes the so-called "antikeratin" Abs and antiperinuclear factor. AFA are the most specific serological markers of RA. We previously showed that they recognize human epidermal filaggrin and other profilaggrin-related proteins of various epithelial tissues. Here, we report further characterization of the protein Ags and epitopes targeted by AFA. All the Ags that exhibit numerous neutral/ acidic isoelectric variants were immunochemically demonstrated to be deiminated proteins. In vitro deimination of a recombinant human filaggrin by a **peptidylarginine deiminase** generated AFA epitopes on the protein. Moreover, two of three filaggrin-derived synthetic peptides with a citrulline in the central position were specifically and widely recognized by AFA affinity-purified from a series of RA sera. These results indicate that citrulline residues are constitutive of the AFA epitopes, but only in the context of specific amino acid sequences of filaggrin. In competition experiments, the two peptides abolished the AFA reactivity of RA sera, showing that they present major AFA epitopes. These data should help in the identification of a putative deiminated AFA-inducing or cross-reactive articular autoantigen and provide new insights into the pathogenesis of RA. They could also open the way toward specific immunosuppressive and/or **preventive therapy** of RA.

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L1                STR
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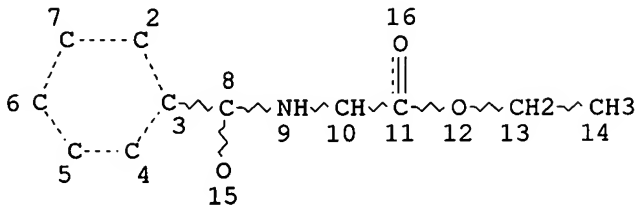


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DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS  15

STEREO ATTRIBUTES: NONE
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100.0% PROCESSED    69409 ITERATIONS                          3916 ANSWERS
SEARCH TIME: 00.00.03


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L1                STR
L2          3916 SEA SSS FUL L1
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                 OR ANTIARTHRIT? OR ANTIRHEUMAT?)
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                 142165-66-0/BI OR 144055-63-0/BI OR 146464-94-0/BI OR
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L9            51 SEA ABB=ON  PLU=ON  L7
L10           24 SEA ABB=ON  PLU=ON  L9 AND (RA(S)ARTHRITIS OR RHEUMATOID?
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L11           24 SEA ABB=ON  PLU=ON  L10 AND (TREAT? OR THERAP? OR PREVENT?)

L12           19 SEA ABB=ON  PLU=ON  L11 NOT (PY=>2004 OR PD=>20040116)
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L13            0 SEA ABB=ON  PLU=ON  L7

     FILE 'REGISTRY' ENTERED AT 10:34:00 ON 21 MAR 2006
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L17           20 SEA ABB=ON  PLU=ON  PEPTIDYLARGININE DEIMINASE ?/CN

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                TID?(1W)DEIMINASE)
L*** DEL      72 S L18 AND (RA(S)ARTHRITIS OR RHEUMATOID? OR ANTIARTHRIT? OR
L*** DEL      20 S L19 AND (TREAT? OR THERAP? OR PREVENT? OR PROPHYLAX? OR P
L*** DEL       3 S L20 NOT (PY=>2004 OR PD=>20040116)
L*** DEL       3 S L21 NOT L6
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                D L22 1-3 .BEVSTR
L*** DEL       1 S L20 AND MARICIC ?/AU
                D KWIC
L19          266 SEA ABB=ON  PLU=ON  L17 OR (PEPTID!LARGININE OR (PROTEIN
                OR PEPTID!L)(W)(ARGININE OR ARG))(W)DEIMINASE OR PAD(S)(PEP
                TID?(1W)DEIMINASE)
L20           72 SEA ABB=ON  PLU=ON  L19 AND (RA(S)ARTHRITIS OR RHEUMATOID?
                OR ANTIARTHRIT? OR ANTIRHEUMAT?)
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L21          20 SEA ABB=ON  PLU=ON  L20 AND (TREAT? OR THERAP? OR PREVENT?
                OR PROPHYLAX? OR PROPHYLACT?)
L*** DEL      1 S L21 AND MARICIC ?/AU
                D KWIC
L22           3 SEA ABB=ON  PLU=ON  L21 NOT (PY=>2004 OR PD=>20040116)
L23           3 SEA ABB=ON  PLU=ON  L22 NOT L6
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                D L23 1-3 .BEVSTR

     FILE 'MEDLINE, BIOSIS, EMBASE, WPIDS, CONFSCI, SCISEARCH,
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L24          48 SEA ABB=ON  PLU=ON  L21
L25          28 DUP REM L24 (20 DUPLICATES REMOVED)
                D 1-28 IBIB ABS

     FILE 'HOME' ENTERED AT 10:55:24 ON 21 MAR 2006
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     provided by InfoChem.

     STRUCTURE FILE UPDATES:   20 MAR 2006  HIGHEST RN 877371-73-8
     DICTIONARY FILE UPDATES:  20 MAR 2006  HIGHEST RN 877371-73-8

     New CAS Information Use Policies, enter HELP USAGETERMS for details.

     TSCA INFORMATION NOW CURRENT THROUGH January 6, 2006

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       conducting SmartSELECT searches.

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     * The CA roles and document type information have been removed from *
     * the IDE default display format and the ED field has been added,   *
     * effective March 20, 2005.  A new display format, IDERL, is now    *
     * available and contains the CA role and document type information. *
     *                                                          *
     ************************************************************

     Structure search iteration limits have been increased.  See HELP SLIMI
     for details.

     REGISTRY includes numerically searchable data for experimental and
     predicted properties as well as tags indicating availability of
     experimental property data in the original document.  For information
     on property searching in REGISTRY, refer to:

     http://www.cas.org/ONLINE/UG/regprops.html

     FILE CAPLUS

     Copyright of the articles to which records in this database refer is
     held by the publishers listed in the PUBLISHER (PB) field (available
     for records published or updated in Chemical Abstracts after December
     26, 1996), unless otherwise indicated in the original publications.
     The CA Lexicon is the copyrighted intellectual property of the
```

FILE COVERS 1907 - 21 Mar 2006 VOL 144 ISS 13
FILE LAST UPDATED: 20 Mar 2006 (20060320/ED)

Effective October 17, 2005, revised CAS Information Use Policies apply They are available for your review at:

http://www.cas.org/infopolicy.html

FILE CAOLD
FILE COVERS 1907-1966
FILE LAST UPDATED: 01 May 1997 (19970501/UP)

This file contains CAS Registry Numbers for easy and accurate substance identification. Title keywords, authors, patent assignees, and patent information, e.g., patent numbers, are now searchable from 1907-1966. TIFF images of CA abstracts printed between 1907-1966 are available in the PAGE display formats.

New CAS Information Use Policies, enter HELP USAGETERMS for details.

This file supports REG1stRY for direct browsing and searching of all substance data from the REGISTRY file. Enter HELP FIRST for more information.

FILE USPATFULL
FILE COVERS 1971 TO PATENT PUBLICATION DATE: 21 Mar 2006 (20060321/PD)
FILE LAST UPDATED: 21 Mar 2006 (20060321/ED)
HIGHEST GRANTED PATENT NUMBER: US7017190
HIGHEST APPLICATION PUBLICATION NUMBER: US2006059596
CA INDEXING IS CURRENT THROUGH 21 Mar 2006 (20060321/UPCA)
ISSUE CLASS FIELDS (/INCL) CURRENT THROUGH: 21 Mar 2006 (20060321/PD)
REVISED CLASS FIELDS (/NCL) LAST RELOADED: Feb 2006
USPTO MANUAL OF CLASSIFICATIONS THESAURUS ISSUE DATE: Feb 2006

FILE MEDLINE
FILE LAST UPDATED: 18 MAR 2006 (20060318/UP). FILE COVERS 1950 TO DA

On December 11, 2005, the 2006 MeSH terms were loaded.

The MEDLINE reload for 2006 is now (26 Feb.) available. For details on the 2006 reload, enter HELP RLOAD at an arrow prompt (=>).
See also:

http://www.nlm.nih.gov/mesh/
http://www.nlm.nih.gov/pubs/techbull/nd04/nd04_mesh.html
http://www.nlm.nih.gov/pubs/techbull/nd05/nd05_med_data_changes.ht
http://www.nlm.nih.gov/pubs/techbull/nd05/nd05_2006_MeSH.html

OLDMEDLINE is covered back to 1950.

MEDLINE thesauri in the /CN, /CT, and /MN fields incorporate the MeSH 2006 vocabulary.

Searcher : Shears 571-272-2528

This file contains CAS Registry Numbers for easy and accurate substance identification.

FILE BIOSIS
FILE COVERS 1969 TO DATE.
CAS REGISTRY NUMBERS AND CHEMICAL NAMES (CNs) PRESENT
FROM JANUARY 1969 TO DATE.

RECORDS LAST ADDED: 15 March 2006 (20060315/ED)

FILE EMBASE
FILE COVERS 1974 TO 20 Mar 2006 (20060320/ED)

EMBASE has been reloaded. Enter HELP RLOAD for details.

EMBASE is now updated daily. SDI frequency remains weekly (default) and biweekly.

This file contains CAS Registry Numbers for easy and accurate substance identification.

FILE MARPAT
FILE CONTENT: 1961-PRESENT VOL 144 ISS 12 (20060317/ED)

SOME MARPAT RECORDS ARE DERIVED FROM INPI DATA FOR 1961-1987

MOST RECENT CITATIONS FOR PATENTS FROM MAJOR ISSUING AGENCIES
(COVERAGE TO THESE DATES IS NOT COMPLETE):

US	2006035965	16 FEB	2006
DE	102004030305	12 JAN	2006
EP	1614691	11 JAN	2006
JP	2006008639	12 JAN	2006
WO	2006012333	02 FEB	2006
GB	2415429	28 DEC	2005
FR	2873371	27 JAN	2006
RU	2267521	10 JAN	2006
CA	2472818	30 DEC	2005

Expanded G-group definition display now available.

New CAS Information Use Policies, enter HELP USAGETERMS for details.

FILE WPIDS
FILE LAST UPDATED: 15 MAR 2006 <20060315/UP>
MOST RECENT DERWENT UPDATE: 200618 <200618/DW>
DERWENT WORLD PATENTS INDEX SUBSCRIBER FILE, COVERS 1963 TO DATE

>>> FOR A COPY OF THE DERWENT WORLD PATENTS INDEX STN USER GUIDE, PLEASE VISIT:
http://www.stn-international.de/training_center/patents/stn_guide.pdf

>>> FOR DETAILS OF THE PATENTS COVERED IN CURRENT UPDATES, SEE
http://scientific.thomson.com/support/patents/coverage/latestupdates/

Searcher : Shears 571-272-2528

>>> FOR INFORMATION ON ALL DERWENT WORLD PATENTS INDEX USER
GUIDES, PLEASE VISIT:
http://scientific.thomson.com/support/products/dwpi/

>>> FAST-ALERTING ACCESS TO NEWLY-PUBLISHED PATENT
DOCUMENTATION NOW AVAILABLE IN DERWENT WORLD PATENTS INDEX
FIRST VIEW - FILE WPIFV.
FOR FURTHER DETAILS:
http://scientific.thomson.com/support/products/dwpifv/

>>> THE CPI AND EPI MANUAL CODES WILL BE REVISED FROM UPDATE 200601.
PLEASE CHECK:
http://scientific.thomson.com/support/patents/dwpiref/reftools/classif

>>> PLEASE BE AWARE OF THE NEW IPC REFORM IN 2006, SEE
http://www.stn-international.de/stndatabases/details/ipc_reform.html
http://scientific.thomson.com/media/scpdf/ipcrdwpi.pdf <<<

FILE CONFSCI
FILE COVERS 1973 TO 25 May 2005 (20050525/ED)

CSA has suspended updates until further notice.

FILE SCISEARCH

FILE COVERS 1974 TO 16 Mar 2006 (20060316/ED)

SCISEARCH has been reloaded, see HELP RLOAD for details.

FILE JICST-EPLUS
FILE COVERS 1985 TO 20 MAR 2006 (20060320/ED)

THE JICST-EPLUS FILE HAS BEEN RELOADED TO REFLECT THE 1999 CONTROLLED
TERM (/CT) THESAURUS RELOAD.

FILE JAPIO
FILE LAST UPDATED: 21 MAR 2006 <20060321/UP>
FILE COVERS APR 1973 TO NOVEMBER 24, 2005

>>> GRAPHIC IMAGES AVAILABLE <<<

>>> NEW IPC8 DATA AND FUNCTIONALITY NOT YET AVAILABLE IN THIS FILE.
USE IPC7 FORMAT FOR SEARCHING THE IPC. WATCH THIS SPACE FOR FURTHE
DEVELOPMENTS AND SEE OUR NEWS SECTION FOR FURTHER INFORMATION
ABOUT THE IPC REFORM <<<

FILE HOME